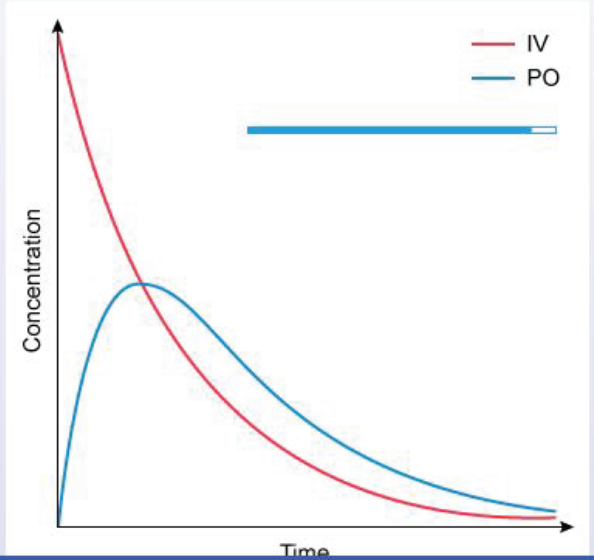
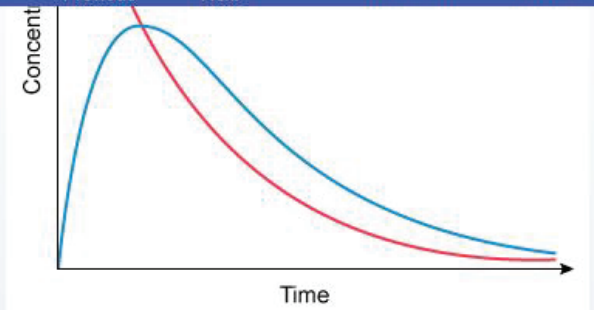
Investigators assessing the bioavailability of a new drug administer it intravenously (IV) to a volunteer and measure plasma concentrations of the drug over time. After the drug is completely cleared from the volunteer's circulation, the investigators administer the same dose of the drug orally (PO) and again measure plasma concentrations of the drug over time. The data obtained are plotted on the graph shown below.





Which of the following is the best determinant of oral bioavailability of this drug?

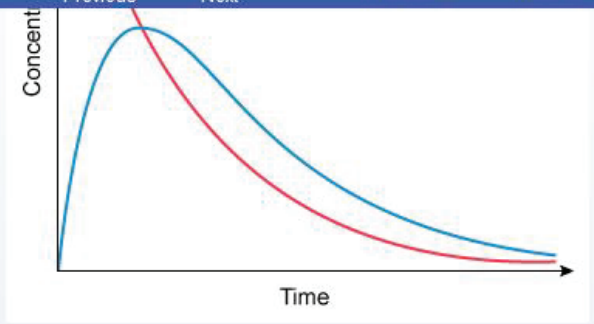
A. Area under the PO curve

B. Area under the PO curve divided by area under the IV curve

C. Maximal concentration at the peak of the PO curve

D. Maximal concentration at the peak of the PO curve divided by maximal concentration at the peak of the IV curve

Submit



Which of the following is the best determinant of oral bioavailability of this drug?

A. Area under the PO curve (34%)

B. Area under the PO curve divided by area under the IV curve (46%)

C. ~~Maximal concentration at the peak of the PO curve~~ (9%)

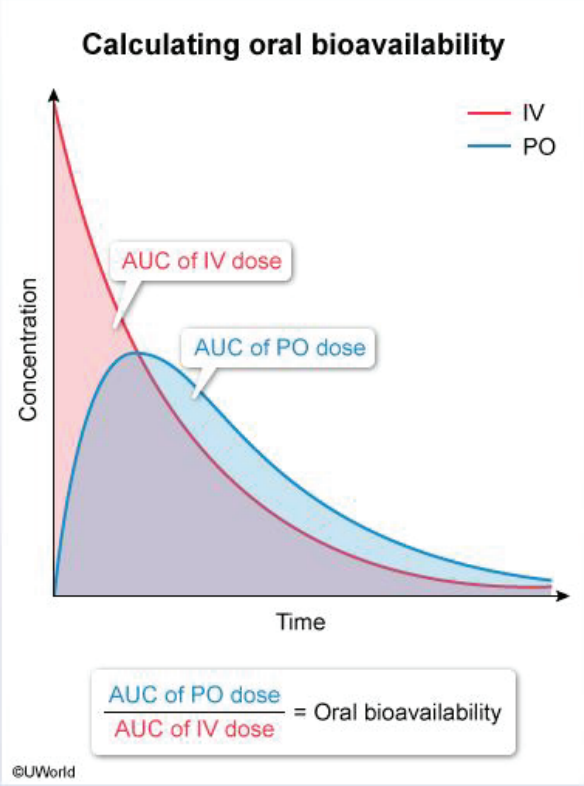
D. ~~Maximal concentration at the peak of the PO curve divided by maximal concentration at the peak of the IV curve~~ (9%)

Correct

46%

01 min, 15 secs

02/14/2021



Bioavailability refers to the fraction of administered drug that reaches the systemic circulation and is

Bioavailability refers to the fraction of administered drug that reaches the systemic circulation and is therefore available for eliciting the desired pharmacologic effect. A drug administered by the intravenous (IV) route has 100% bioavailability by definition. For other modes of drug administration (eg, oral [PO], intramuscular [IM], subcutaneous [SQ], transdermal [TD], rectal [PR]), the bioavailability is usually less than 100%.

The bioavailability of a drug for a given route of administration can be determined by plotting plasma drug concentrations over time for a given dose administered by both the IV route and the other route being studied (eg, PO). The **area under the curve** (AUC) of each plot represents the **total systemic drug exposure** for the given dose and route **(Choice A)**. Bioavailability can then be determined by comparing the AUCs of each curve. In this case, PO bioavailability can be calculated by **dividing the AUC of the PO curve by the AUC of the IV curve**.

In the case of PO administration, bioavailability depends upon the drug's ability to cross the intestinal mucosa and can be influenced by gastric acidity and motility, the presence of food or other drugs in the gut, and first-pass metabolism by the intestine and liver.

(Choice C) The maximal concentration at the peak of the PO curve (ie, peak plasma level) is dose dependent and is not an indicator of drug bioavailability.

(Choice C) The maximal concentration at the peak of the PO curve (ie, peak plasma level) is dose dependent and is not an indicator of drug bioavailability.

(Choice D) PO administration of a drug usually results in lower peak serum drug levels compared to IV administration, even when PO bioavailability is near 100%, due to delayed absorption from the gastrointestinal tract (versus near-instantaneous delivery of IV drugs). As a result, comparing peak PO to peak IV concentration levels is not an appropriate way to determine bioavailability.

Educational objective:

Bioavailability refers to the fraction of administered drug that reaches the systemic circulation. For a drug administered by any route other than intravenous (IV), bioavailability is usually less than 100%. Bioavailability can be determined by graphing plasma drug concentrations over time for a given dose administered by both the IV route and the other route being studied. Oral (PO) bioavailability is calculated by dividing the area under the PO curve by the area under the IV curve.

Pharmacology	Miscellaneous (Multisystem)	Route of administration & bioavailability
Subject	System	Topic

A 46-year-old man comes to the emergency department due to recurrent nosebleeds. When interviewed for additional history, he becomes belligerent and uncooperative. The patient has a history of alcohol abuse and chronic mental illness. He has been placed in homeless shelters on multiple occasions but has not remained there for any prolonged periods. Physical examination shows swollen gums, scattered ecchymoses, and hyperkeratosis. He also has a chronic ulcer on the left lower extremity that does not appear to be infected. Which of the following mechanisms accounts for this patient's examination findings?

A. Abnormal oxidative decarboxylation of ketoacids
B. Abnormal proline hydroxylation
C. Abnormal transamination
D. Deficient methionine synthesis
E. Diminished synthesis of purines

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 46-year-old man comes to the emergency department due to recurrent nosebleeds. When interviewed for additional history, he becomes belligerent and uncooperative. The patient has a history of alcohol abuse and chronic mental illness. He has been placed in homeless shelters on multiple occasions but has not remained there for any prolonged periods. Physical examination shows swollen gums, scattered ecchymoses, and hyperkeratosis. He also has a chronic ulcer on the left lower extremity that does not appear to be infected. Which of the following mechanisms accounts for this patient's examination findings?

A. Abnormal oxidative decarboxylation of ketoacids (4%)
✓ B. Abnormal proline hydroxylation (80%)
C. Abnormal transamination (4%)
D. Deficient methionine synthesis (5%)
E. Diminished synthesis of purines (4%)

Correct

80%
Answered correctly

57 secs
Time Spent

01/21/2021
Last Updated

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Water-soluble vitamins

Vitamin	Primary function	Deficiency
B_1 (thiamine)	Decarboxylation of α-keto acids (carbohydrate metabolism)	• Beriberi (peripheral neuropathy, heart failure) • Wernicke-Korsakoff syndrome
B_2 (riboflavin)	Mitochondrial electron carrier (FMN, FAD)	• Angular cheilosis, stomatitis, glossitis • Normocytic anemia
B_3 (niacin)	Electron transfer reactions (NAD/NADP)	• Pellagra (dermatitis, dementia, diarrhea) • Peripheral neuropathy
B_6 (pyridoxine)	Transamination of amino acids (amino acid synthesis)	• Cheilosis, stomatitis, glossitis
B_9 (folate, folic acid)	Hydroxymethyl/formyl carrier (purine & thymine synthesis)	• Megaloblastic anemia • Neural tube defects (fetus)
B_{12} (cobalamin)	Isomerase & methyltransferase cofactor (DNA & methionine synthesis)	• Megaloblastic anemia • Neurologic deficits
C (ascorbic acid)	Hydroxylation of proline & lysine (collagen synthesis)	• Scurvy

Zoom In | Zoom Out | Reset | New | Existing | My Notebook

carrier (purine & thymine

In the United States, **vitamin C deficiency (scurvy)** is most often seen in severely malnourished individuals (eg, homeless, alcohol or drug abusers). Symptoms of vitamin C deficiency are the result of decreased connective tissue strength. The capillary walls are especially fragile, leading to **easy bruising**, mucosal bleeding, and perifollicular petechial hemorrhages. Patients may also suffer from **periodontal disease** (gum swelling, loosening of the teeth, and infection) and **poor wound healing**, and have **hyperkeratotic follicles** with corkscrew hairs. Scurvy is even more severe in children and manifests with hemorrhages, bony deformities, and subperiosteal and joint hematomas.

Vitamin C is necessary for the **hydroxylation of proline and lysine** residues during collagen synthesis. This reaction is executed by prolyl and lysyl hydroxylases, with vitamin C serving as a reducing agent. Hydroxyproline and hydroxylysine are essential for cross-linking collagen molecules. In scurvy, collagen cross-linking is compromised, thereby greatly reducing its tensile strength.

(Choice A) Thiamine (vitamin B_1) serves as a coenzyme in the decarboxylation reactions mediated by several dehydrogenase enzymes. It is necessary for the conversions of pyruvate to acetyl-CoA and of alpha-ketoglutarate to succinyl-CoA in the citric acid cycle. Vitamin B_1 deficiency can cause peripheral neuropathy, heart failure, and central nervous system dysfunction (Wernicke-Korsakoff syndrome).

(Choice C) Vitamin B$_6$ (pyridoxine) serves as a cofactor in many reactions that involve amino acids (eg

alpha-ketoglutarate to succinyl-CoA in the citric acid cycle. Vitamin B_1 deficiency can cause peripheral neuropathy, heart failure, and central nervous system dysfunction (Wernicke-Korsakoff syndrome).

(Choice C) Vitamin B_6 (pyridoxine) serves as a cofactor in many reactions that involve amino acids (eg, transamination, decarboxylation, deamination). Pyridoxine deficiency manifests with seborrheic dermatitis, glossitis, and peripheral neuropathy.

(Choice D) Vitamin B_{12} is necessary for the synthesis of methionine from homocysteine and for the synthesis of succinyl-CoA from methylmalonyl-CoA. Deficiency of vitamin B_{12} causes megaloblastic anemia and subacute combined degeneration of the spinal cord.

(Choice E) Purine and thymidine synthesis is diminished in patients with folate deficiency. The resultant decreased ability of erythropoietic cells to form DNA causes megaloblastic anemia.

Educational objective:
Vitamin C is necessary for the hydroxylation of proline and lysine residues in pro-collagen. Vitamin C deficiency (scurvy) is most often seen in severely malnourished individuals and leads to capillary bleeding, poor wound healing, and periodontal disease. In children, bony deformities and subperiosteal hemorrhages are also characteristic.

References

A 2-year-old boy is brought to the office due to fever. For the past 6 days, he has had a fever of 39 C (102.2 F) to 40 C (104 F) that subsides minimally with acetaminophen. Yesterday, his mother noted a rash on his diaper area. Temperature is 39.2 C (102.6 F), pulse is 140/min, and respirations are 30/min. Physical examination shows an irritable boy. The patient's neck is supple with full range of motion. Both hands and feet are slightly erythematous and edematous, and a peeling rash is present over the perineal area. His eyes and lips appear as shown. The remainder of the examination is unremarkable. Which of the following is the most likely diagnosis?

A. Adenovirus infection
B. Hand, foot, and mouth disease
C. Kawasaki disease
D. Measles
E. Scarlet fever

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Zoom In
Zoom Out
Reset
New | Existing
My Notebook

1
2
• 3
• 4
• 5
• 6
• 7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

Exhibit Display

Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

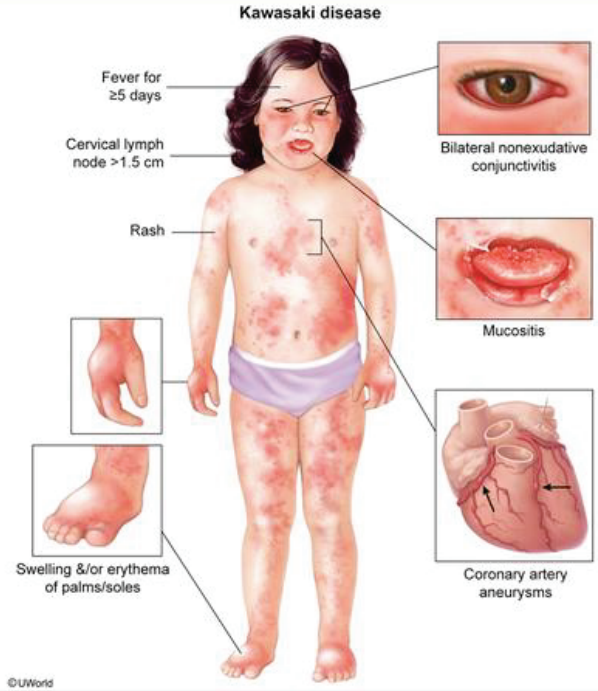
A 2-year-old boy is brought to the office due to fever. For the past 6 days, he has had a fever of 39 C (102.2 F) to 40 C (104 F) that subsides minimally with acetaminophen. Yesterday, his mother noted a rash on his diaper area. Temperature is 39.2 C (102.6 F), pulse is 140/min, and respirations are 30/min. Physical examination shows an irritable boy. The patient's neck is supple with full range of motion. Both hands and feet are slightly erythematous and edematous, and a peeling rash is present over the perineal area. His eyes and lips appear as shown. The remainder of the examination is unremarkable. Which of the following is the most likely diagnosis?

A. Adenovirus infection (4%)
B. Hand, foot, and mouth disease (19%)
✓ C. Kawasaki disease (63%)
D. Measles (3%)
E. Scarlet fever (8%)

63%
01 min, 17 secs
01/16/2021

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

This patient has **Kawasaki disease**, an acute, inflammatory condition characterized by vasculitis of medium-sized arteries. Most cases occur in children **age <5** with a peak incidence among those of East Asian ethnicity. The persistent release of proinflammatory cytokines causes irritability and a **prolonged high fever** that is often unresponsive to antipyretics.

Diagnosis is clinical, consisting of fever ≥5 days and ≥4 of the following findings:

- **Conjunctivitis**: bilateral, nonexudative, limbus sparing
- **Mucositis**: erythematous, fissured lips; strawberry tongue
- Rash: polymorphous, often begins in perineal area
- **Distal extremity changes**: erythema, edema, desquamation of the hands and feet
- Cervical lymphadenopathy

A serious complication of Kawasaki disease is coronary artery inflammation leading to the development of **coronary artery aneurysms**, which can lead to myocardial ischemia, arrhythmias, and sudden death.

(Choice A) Pharyngoconjunctival fever due to adenovirus can present with prolonged fever and nonexudative conjunctivitis. In contrast to this case, however, patients typically have pharyngitis, not

(Choice A) Pharyngoconjunctival fever due to adenovirus can present with prolonged fever and nonexudative conjunctivitis. In contrast to this case, however, patients typically have pharyngitis, not mucositis of the lips, and edematous extremities are not seen.

(Choice B) Hand, foot, and mouth disease caused by coxsackievirus presents with fever and rash on the palms and soles. However, discrete oropharyngeal sores would be seen, and conjunctivitis and extremity edema would not be expected.

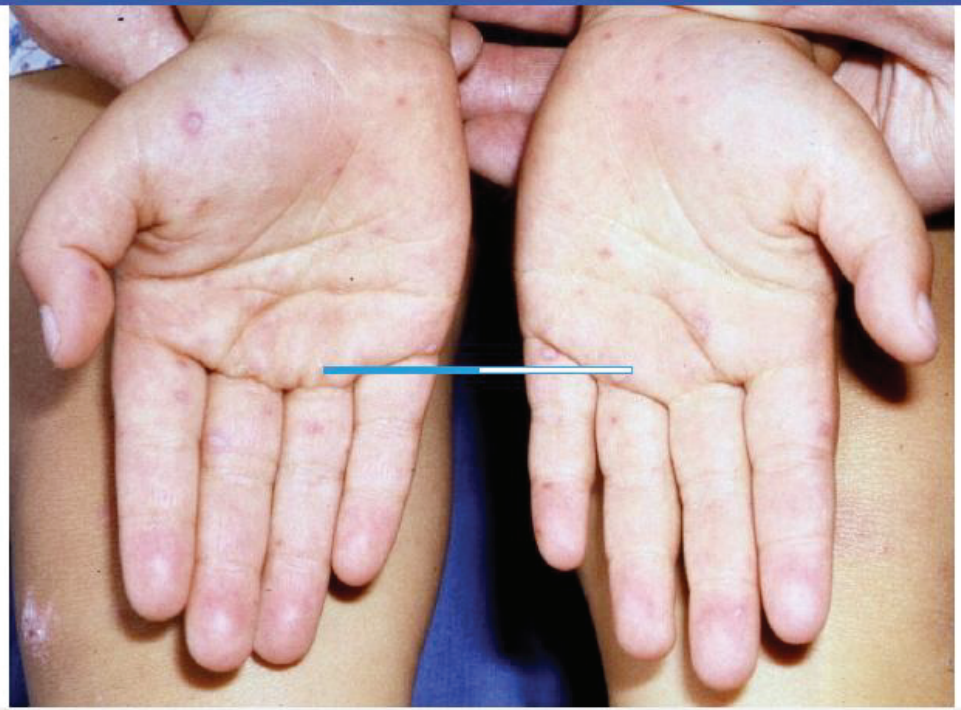
(Choice D) In addition to conjunctivitis and fever, measles causes cough and coryza, neither of which is seen here. Oropharyngeal examination may reveal Koplik spots, or discrete buccal lesions, not diffuse labial erythema and inflammation. In addition, the measles rash is characterized by cephalocaudal spread of maculopapular lesions that subsequently darken and coalesce; this patient's isolated perineal rash is inconsistent with measles.

(Choice E) Scarlet fever presents with fever, strawberry tongue, and rash. Although the rash in scarlet fever can desquamate, it is sandpaper-textured, diffuse, and prominent along skin folds (eg, axillae, antecubital fossae). Moreover, exudative pharyngitis is usually present, and conjunctivitis would not be expected.

Educational objective:

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

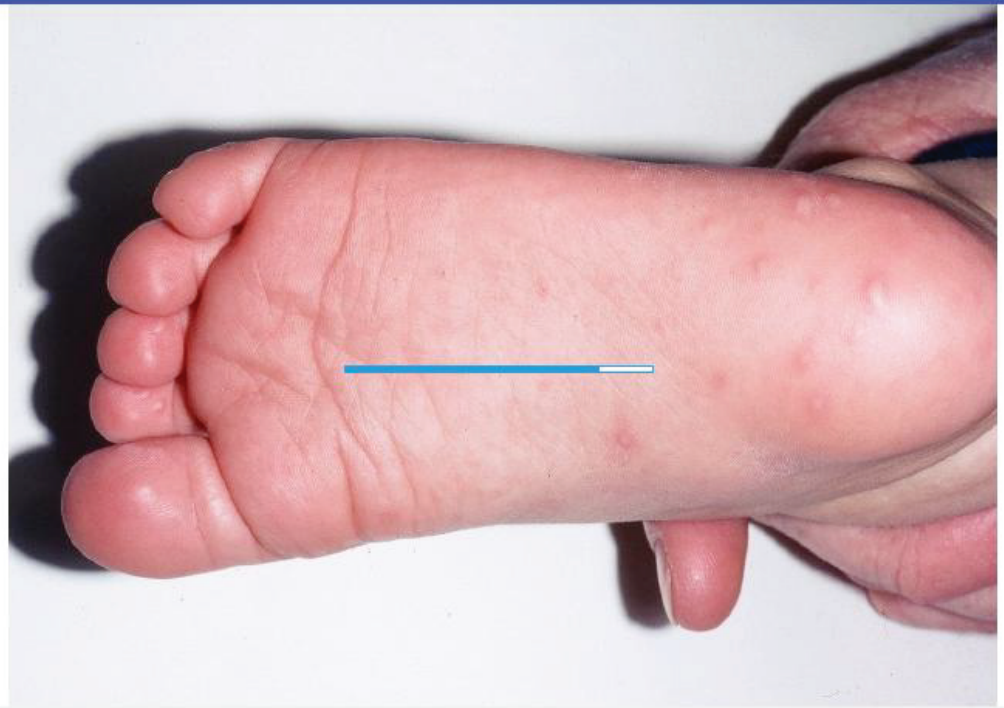


Zoom In | Zoom Out | Reset | New | Existing | My Notebook

Educational objective:

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

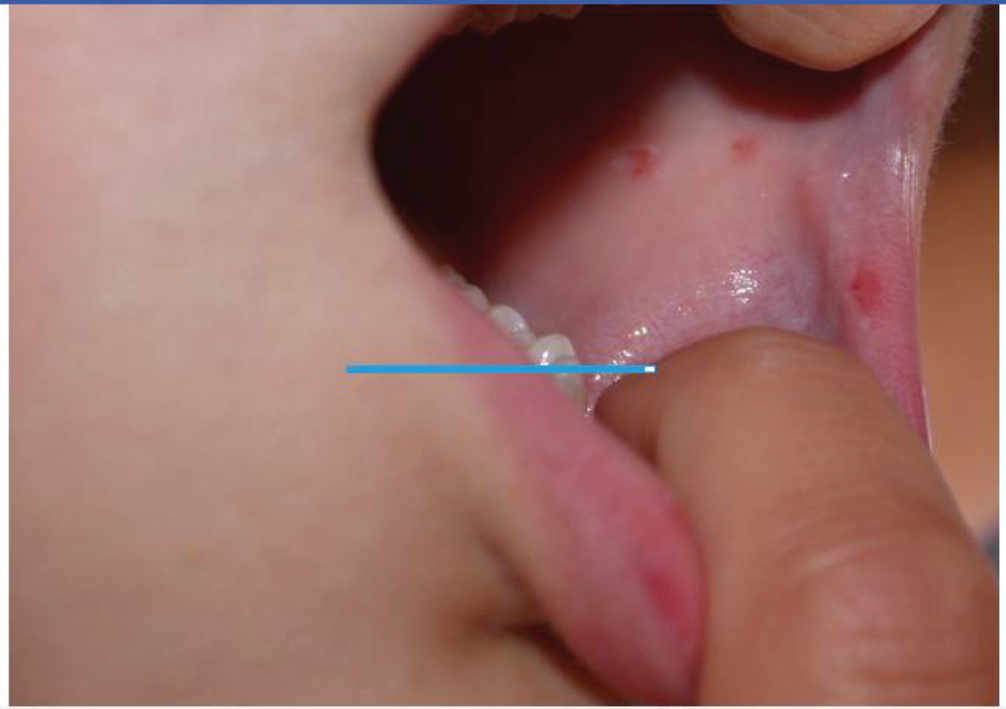


Zoom In | Zoom Out | Reset | New | Existing | My Notebook

Educational objective:

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

Educational objective:

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

edema would not be expected.

(Choice D) In addition to conjunctivitis and fever, measles causes cough and coryza, neither of which is seen here. Oropharyngeal examination may reveal Koplik spots, or discrete buccal lesions, not diffuse labial erythema and inflammation. In addition, the measles rash is characterized by cephalocaudal spread of maculopapular lesions that subsequently darken and coalesce; this patient's isolated perineal rash is inconsistent with measles.

(Choice E) Scarlet fever presents with fever, strawberry tongue, and rash. Although the rash in scarlet fever can desquamate, it is sandpaper-textured, diffuse, and prominent along skin folds (eg, axillae, antecubital fossae). Moreover, exudative pharyngitis is usually present, and conjunctivitis would not be expected.

Educational objective:
Kawasaki disease is a vasculitis characterized by fever for ≥5 days and ≥4 of the following findings: nonexudative conjunctivitis, extremity changes, cervical lymphadenopathy, mucositis, and polymorphous rash.

References

- Diagnosis and management of Kawasaki disease.

An 80-year-old woman is brought to the emergency department following a burn injury. The patient lives alone in an apartment. Earlier today, her clothes caught fire while she was cooking. The patient's neighbor heard her screaming and helped extinguish the fire, but the patient had already sustained burns on her face, arms, and body. She has a history of Parkinson disease and osteoporosis. Temperature is 37.4 C (99.3 F), blood pressure is 140/84 mm Hg, pulse is 110/min, and respirations are 18/min. Oxygen saturation is 95% on room air. On examination, the patient is in distress and anxious. There are partial- to full-thickness burns involving the lower face, neck, both arms, and anterior chest and abdomen. Which of the following age-related cardiopulmonary changes is most likely to increase this patient's mortality risk?

A. Decreased cardiac adrenergic response
B. Decreased left ventricular wall thickness
C. Decreased ventilation-perfusion mismatch
D. Increased diaphragmatic strength
E. Increased large artery compliance
F. Increased lung gas exchange surface area

1
2
3
4
• 5
• 6
• 7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

heard her screaming and helped extinguish the fire, but the patient had already sustained burns on her face, arms, and body. She has a history of Parkinson disease and osteoporosis. Temperature is 37.4 C (99.3 F), blood pressure is 140/84 mm Hg, pulse is 110/min, and respirations are 18/min. Oxygen saturation is 95% on room air. On examination, the patient is in distress and anxious. There are partial- to full-thickness burns involving the lower face, neck, both arms, and anterior chest and abdomen. Which of the following age-related cardiopulmonary changes is most likely to increase this patient's mortality risk?

✓ A. Decreased cardiac adrenergic response (72%)

✗ B. Decreased left ventricular wall thickness (6%)

C. ~~Decreased ventilation-perfusion mismatch~~ (8%)

D. ~~Increased diaphragmatic strength~~ (0%)

E. Increased large artery compliance (7%)

F. ~~Increased lung gas exchange surface area~~ (3%)

Incorrect
Correct answer

72%

04 mins, 04 secs

02/22/2021

Physiologic age-related cardiovascular changes	
Aortic stiffening	• Loss of elastin, ↑ collagen deposition • ↑ Pulse pressure (isolated systolic HTN)
Mild concentric LVH*	• Response to cardiomyocyte dropout & ↑ afterload • Resting EF, SV & cardiac output maintained • ↓ Maximal cardiac output
Conduction cell degeneration	• Slightly ↓ resting heart rate • ↓ Maximal heart rate
Reduced baroreceptor sensitivity & adrenergic responsiveness	• ↑ Orthostasis • ↓ Heart rate & contractility response • ↑ Circulating catecholamines

*A soft S4 is a normal finding in the elderly.

EF = ejection fraction; **HTN** = hypertension; **LVH** = left ventricular hypertrophy; **SV** = stroke volume.

With **advancing age**, the cardiopulmonary system undergoes physiologic changes that can lead to

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

EF = ejection fraction; **HTN** = hypertension; **LVH** = left ventricular hypertrophy; **SV** = stroke volume.

With **advancing age**, the cardiopulmonary system undergoes physiologic changes that can lead to reduced ability to cope with critical illness (eg, severe burns). One of the major changes in the cardiovascular system involves **decreased responsiveness to adrenergic stimuli**, which contributes to a lower maximal heart rate and **reduced maximal cardiac output**.

Critical illness often involves a **hypermetabolic state** (ie, increased resting energy expenditure) and a marked decrease in intravascular blood volume (eg, evaporative losses with severe burn injury, vascular leakage with sepsis), both of which necessitate a sympathetic-mediated increase in heart rate and contractility to help maintain organ and tissue perfusion. The attenuation of this response with age likely contributes to poorer critical illness outcomes in elderly patients.

(Choices B and E) Compliance of the aorta and other large arteries decreases with age, resulting in isolated systolic hypertension and an increase in left ventricular afterload. In response to the increased afterload, mild concentric left ventricular hypertrophy occurs, resulting in increased left ventricular wall thickness. The reduced arterial compliance also decreases blood volume retained in the arterial system, which increases susceptibility to hypotension during critical illness.

(Choices C and F) Degeneration of lung elastin with age causes alveolar enlargement and increased air

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

thickness. The reduced arterial compliance also decreases blood volume retained in the arterial system, which increases susceptibility to hypotension during critical illness.

(Choices C and F) Degeneration of lung elastin with age causes alveolar enlargement and increased air trapping. The alveolar enlargement decreases the percentage of the alveolar surface in contact with alveolar capillaries, reducing gas exchange surface area. This effect, combined with reduced alveolar ventilation due to increased air trapping, increases ventilation-perfusion mismatching.

(Choice D) Diaphragmatic strength decreases with age. This has little effect on resting tidal volumes, but it increases the susceptibility to respiratory fatigue during periods of respiratory stress (eg, critical illness).

Educational objective:
Physiologic age-related changes in the cardiopulmonary system can lead to reduced ability to cope with critical illness. These changes include reduced maximal heart rate and cardiac output due to decreased responsiveness to adrenergic stimuli, reduced retention of arterial blood volume due to decreased arterial compliance, and reduced respiratory strength and gas exchange efficiency.

Pathophysiology	Miscellaneous (Multisystem)	Aging
Subject	System	Topic

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A newborn is examined immediately after an induced vaginal delivery for fetal growth retardation. On visual inspection, the infant has low-set ears, a small mandible, and a prominent occiput. The neonate has a weak cry and increased tone of the extremities, including clenched hands with second and fifth digits on top of the third and fourth digits. Cardiac auscultation reveals a harsh, IV/VI holosystolic murmur heard best at the left sternal border. The infant is transferred to the neonatal intensive care unit for further workup and management. Which of the following is the most likely chromosomal abnormality in this infant?

A. 5p deletion
B. 22q11 deletion
C. 47, XX, +13
D. 47, XX, +18
E. 47, XX, +21

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A newborn is examined immediately after an induced vaginal delivery for fetal growth retardation. On visual inspection, the infant has low-set ears, a small mandible, and a prominent occiput. The neonate has a weak cry and increased tone of the extremities, including clenched hands with second and fifth digits on top of the third and fourth digits. Cardiac auscultation reveals a harsh, IV/VI holosystolic murmur heard best at the left sternal border. The infant is transferred to the neonatal intensive care unit for further workup and management. Which of the following is the most likely chromosomal abnormality in this infant?

A. 5p deletion (7%)
B. 22q11 deletion (7%)
C. 47, XX, +13 (13%)
D. 47, XX, +18 (64%)
E. 47, XX, +21 (6%)

Correct

64%
Answered correctly

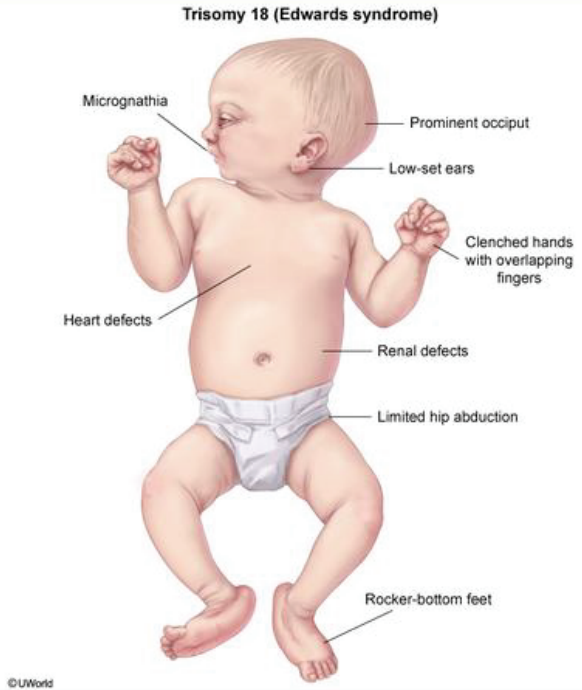
01 min, 07 secs
Time Spent

03/09/2021
Last Updated

1
2
3
4
5
• 6
• 7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

Explanation

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

This patient has **trisomy 18 (Edwards syndrome)**, in which a complete extra copy of chromosome 18 is inherited as a result of **meiotic nondisjunction**. This error in oocyte division occurs prior to ovulation and fertilization and increases with maternal age ≥35.

Dysmorphic features include micrognathia, low-set ears, prominent occiput, and **rocker bottom feet**. Patients have significant hypertonia, including **clenched hands** with **overlapping fingers**. Anomalies of cardiac (eg, **ventricular septal defect**, patent ductus arteriosus), genitourinary (eg, horseshoe kidney), and gastrointestinal (eg, Meckel's diverticulum, malrotation) systems are characteristic. Prenatal ultrasound findings include fetal growth restriction, as seen in this patient. The majority of those affected die in utero; half of livebirths die by age 2 weeks. Surviving patients have severe intellectual disability.

(Choice A) Cri-du-chat syndrome (5p deletion) presents with a weak or "cat-like" cry as well as hypotonia, failure to thrive, and developmental delay. Phenotypic features include microcephaly, low-set ears, hypertelorism, and a broad nasal bridge.

(Choice B) Features of DiGeorge syndrome (22q11 deletion) include aortic arch anomalies, thymic hypoplasia/aplasia, and hypocalcemia (parathyroid gland underdevelopment). Phenotypically, neonates can present with hypertelorism, low-set ears, micrognathia, and cleft palate.

hypertelorism, and a broad nasal bridge.

(Choice B) Features of DiGeorge syndrome (22q11 deletion) include aortic arch anomalies, thymic hypoplasia/aplasia, and hypocalcemia (parathyroid gland underdevelopment). Phenotypically, neonates can present with hypertelorism, low-set ears, micrognathia, and cleft palate.

(Choice C) Trisomy 13 (Patau syndrome) presents with midline facial defects (eg, holoprosencephaly, cleft lip/palate), musculoskeletal abnormalities (eg, polydactyly), and gastrointestinal anomalies (eg, omphalocele, umbilical hernia). Trisomy 13 is notably not associated with overlapping fingers.

(Choice E) Trisomy 21 (Down syndrome) is the most common autosomal trisomy. Classic findings include a flat facial profile, upslanting palpebral fissures, low-set small ears, single transverse palmar crease, and hypotonia.

Educational objective:

Trisomy 18, or Edwards syndrome, is most commonly the result of meiotic nondisjunction due to advanced maternal age. Key findings include fetal growth retardation, hypertonia (clenched hands with overlapping fingers), rocker bottom feet, and cardiac/gastrointestinal/renal defects.

References

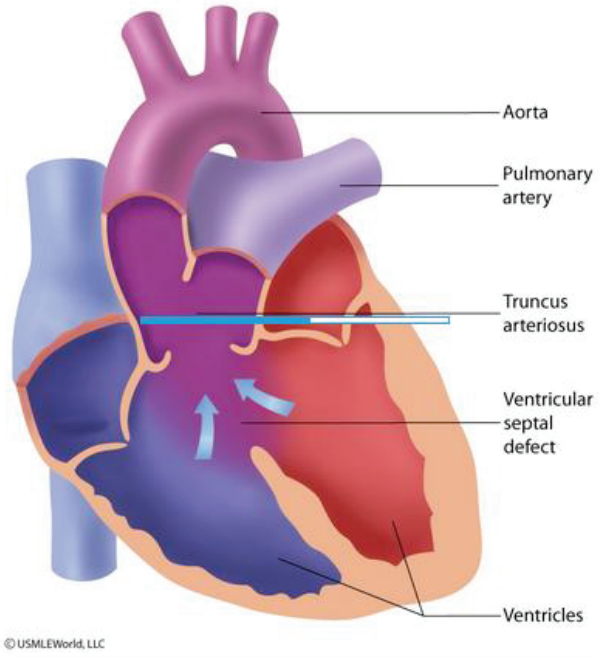
- The trisomy 18 syndrome.

1
2
3
4
5
• 6
• 7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

hypertelorism, and a broad nasal bridge.

Exhibit Display

Truncus arteriosus



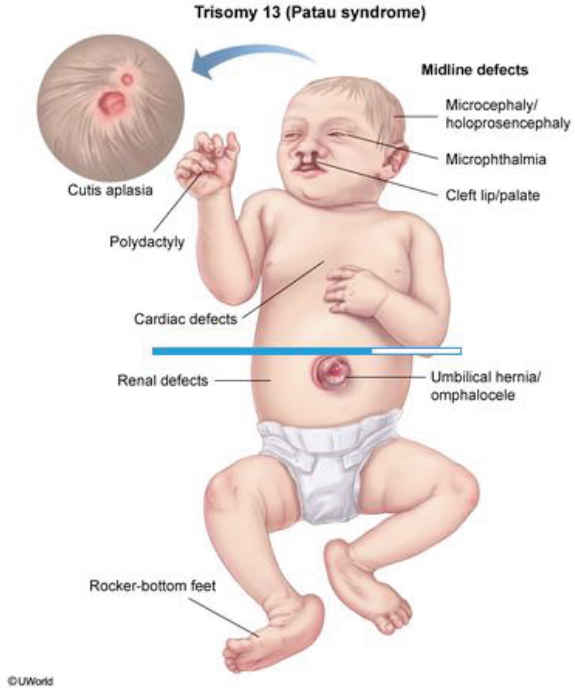
Zoom In | Zoom Out | Reset | New | Existing | My Notebook

• The trisomy 18 syndrome.

1
2
3
4
5
• 6
• 7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

hypertelorism, and a broad nasal bridge.

Exhibit Display



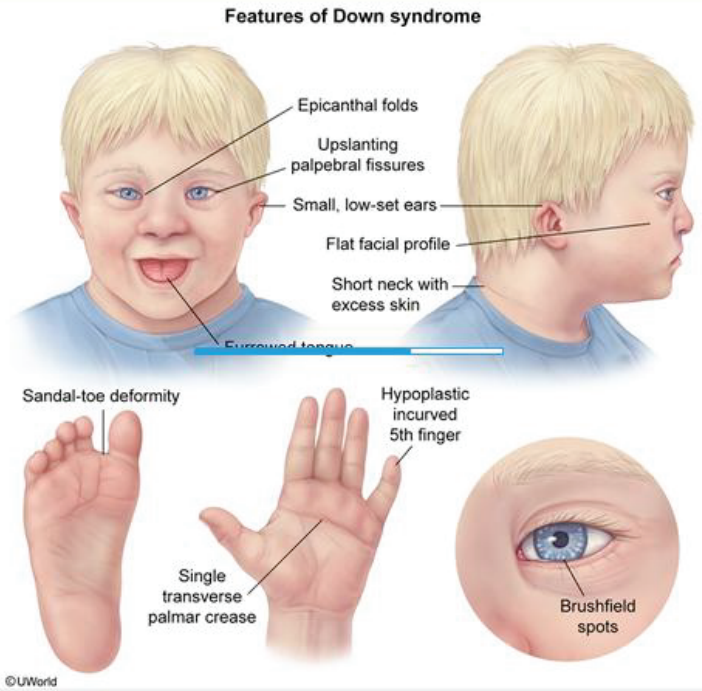
Zoom In | Zoom Out | Reset | New | Existing | My Notebook

• The trisomy 18 syndrome.

1
2
3
4
5
• 6
• 7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

hypertelorism, and a broad nasal bridge.

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

• The trisomy 18 syndrome.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 23-year-old healthy man who lives at sea level is attempting to trek to the Mount Everest base camp at an elevation of 5,334 m (17,500 ft). While hiking, he experiences mild shortness of breath, lightheadedness, headache, and fatigue. The patient reaches the base camp after 7 days, where he is evaluated at a high-altitude clinic. He appears exhausted, but physical examination is otherwise unrevealing. Which of the following physiologic changes has most likely occurred in this patient?

A. Decreased peripheral chemoreceptor firing
B. Decreased pulmonary vascular resistance
C. Decreased renal erythropoietin production
D. Increased erythrocyte 2,3-bisphosphoglycerate (2,3-BPG) synthesis
E. Increased renal HCO_3^- reabsorption

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 23-year-old healthy man who lives at sea level is attempting to trek to the Mount Everest base camp at an elevation of 5,334 m (17,500 ft). While hiking, he experiences mild shortness of breath, lightheadedness, headache, and fatigue. The patient reaches the base camp after 7 days, where he is evaluated at a high-altitude clinic. He appears exhausted, but physical examination is otherwise unrevealing. Which of the following physiologic changes has most likely occurred in this patient?

A. ~~Decreased peripheral chemoreceptor firing~~ (4%)
B. Decreased pulmonary vascular resistance (3%)
C. ~~Decreased renal erythropoietin production~~ (1%)
✓ D. Increased erythrocyte 2,3-bisphosphoglycerate (2,3-BPG) synthesis (81%)
E. ~~Increased renal HCO_3^- reabsorption~~ (9%)

Correct

81%
Answered correctly

02 mins, 52 secs
Time Spent

10/24/2020
Last Updated

High-altitude illness	
Pathogenesis	• Reduced PiO_2 at high altitude (>2,500 m [~8000 ft])
Physiologic responses	• Hyperventilation: helps ↑ PaO_2 but causes ↓ $PaCO_2$ • Erythrocytes: ↑ 2,3-BPG production (↑ O_2 unloading in tissues) • Kidneys: ↑ Erythropoietin production & ↑ HCO_3^- excretion
Complications	• Acute mountain sickness ◦ Headache, fatigue, nausea • Cerebral edema (↓ PaO_2 → ↑ cerebral blood flow) ◦ Lethargy, confusion, gait disturbance • Pulmonary edema (unbalanced hypoxic

responses	O_2 unloading in tissues) • Kidneys: ↑ Erythropoietin production & ↑ HCO_3^- excretion
Complications	• Acute mountain sickness ◦ Headache, fatigue, nausea • Cerebral edema (↓ PaO_2 → ↑ cerebral blood flow) ◦ Lethargy, confusion, gait disturbance • Pulmonary edema (unbalanced hypoxic vasoconstriction) ◦ Dyspnea, cough ± hemoptysis, respiratory distress

2,3-BPG = 2,3-bisphosphoglycerate; **PiO_2** = partial pressure of inspired oxygen.

This patient is most likely suffering from **acute mountain sickness (AMS)**, a type of **high-altitude illness** resulting from low partial pressure of oxygen (pO_2) in environments >2,500 m (8,000 ft). Although the

This patient is most likely suffering from **acute mountain sickness (AMS)**, a type of **high-altitude illness** resulting from low partial pressure of oxygen (pO_2) in environments >2,500 m (8,000 ft). Although the fraction of oxygen in inspired air remains constant (21%) at different terrestrial elevations, barometric pressure drops with increasing altitude, leading to decreased pO_2 in the air and lungs.

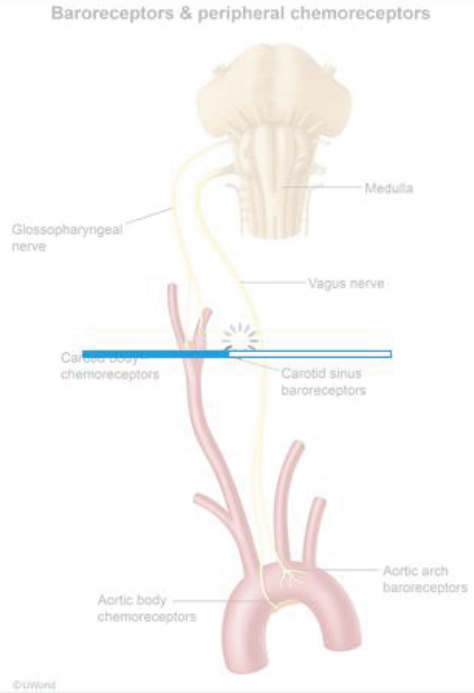
In an otherwise healthy patient, the pO_2 rapidly equilibrates between the alveoli and arterial blood, causing **hypoxemia** when the pO_2 drops below 80 mm Hg. Several acute physiological changes occur in response to the resulting **hypobaric hypoxia**:

- Increased firing of peripheral chemoreceptors causes hyperventilation, which directly reduces hypoxemia and improves tissue oxygenation **(Choice A)**.
- **Increased 2,3-bisphosphoglycerate (2,3-BPG)** synthesis by erythrocytes, which shifts the O_2-hemoglobin dissociation curve to the right, decreasing the affinity of hemoglobin for oxygen and facilitating the offloading of oxygen in peripheral tissues.

Hyperventilation also decreases the partial pressure of carbon dioxide, resulting in increased blood pH (**respiratory alkalosis**). Common symptoms of AMS include headache, fatigue, dyspnea, dizziness, and sleep disturbances. Most cases subside within 2 days but can progress to life-threatening cerebral and/or

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

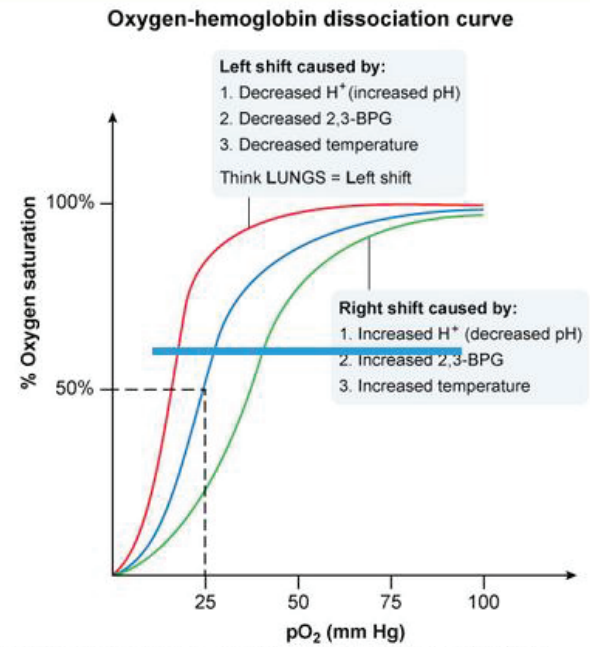
Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



2,3-BPG = 2,3-bisphosphoglycerate; pO_2 = partial pressure of oxygen in the blood.

Zoom In | Zoom Out | Reset | New | Existing | My Notebook

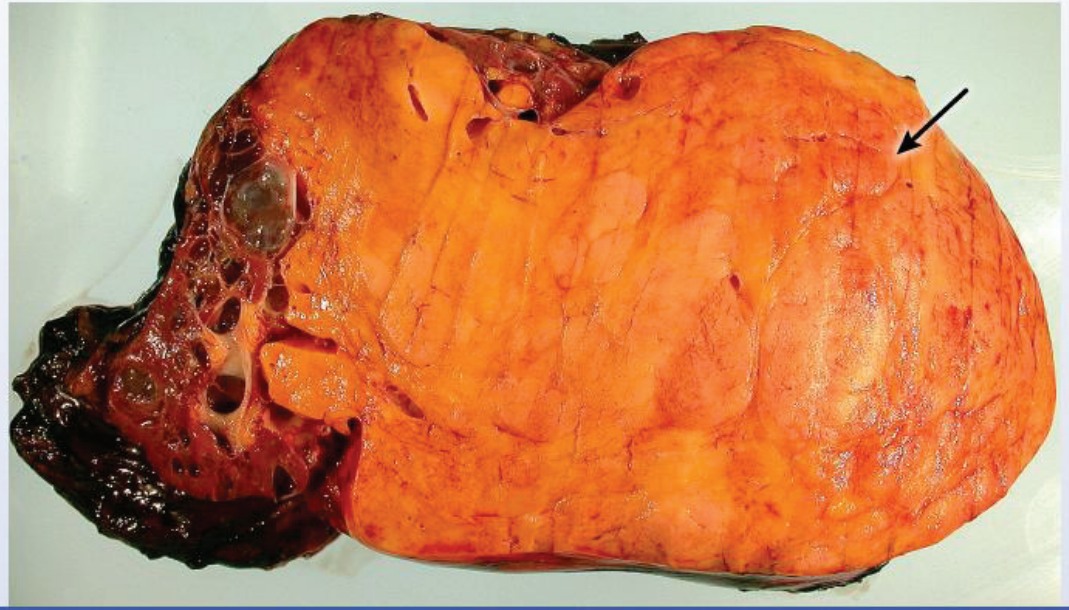
Hyperventilation also decreases the partial pressure of carbon dioxide, resulting in increased blood pH (**respiratory alkalosis**). Common symptoms of AMS include headache, fatigue, dyspnea, dizziness, and sleep disturbances. Most cases subside within 2 days but can progress to life-threatening cerebral and/or pulmonary edema in susceptible patients. In the absence of underlying pathology, symptoms typically resolve within 48 hours as the kidneys **increase HCO_3^- excretion** to compensate for the alkalosis, restoring pH toward the normal range and improving symptoms **(Choice E)**.

(Choice B) Hypoxia induces widespread vasoconstriction of the pulmonary vasculature; this increases pulmonary vascular resistance and pulmonary arterial pressure and can result in pulmonary edema.

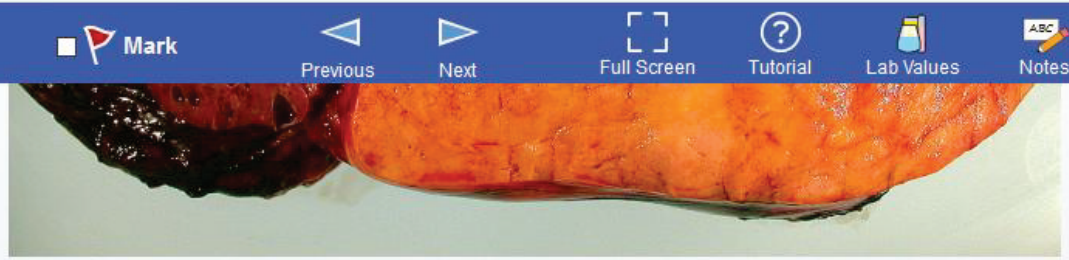
(Choice C) Hypoxemia stimulates increased erythropoietin production in the renal cortex, which results in polycythemia and increased oxygen-carrying capacity over time (days to weeks of sustained hypoxemia).

Educational objective:
People traveling to elevations >2500 m (8000 ft) can develop high-altitude illness, characterized by hypobaric hypoxia with the potential to develop life-threatening cerebral and/or pulmonary edema. Key adaptive responses to hypoxemia include hyperventilation to increase blood oxygenation and increased synthesis of 2,3-bisphosphoglycerate in erythrocytes (facilitating oxygen offloading into peripheral tissues).

A 32-year-old woman is evaluated for pain and a mass in the right flank. Imaging studies reveal a large mass arising from the right kidney and similar smaller masses in the left kidney. Surgery to remove the right-sided tumor along with the right kidney is performed; the cut section specimen is shown in the image below.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16



Histopathologic evaluation shows that the mass is composed of fat, smooth muscle, and blood vessels.

This patient is most likely to have which of the following additional findings?

A. Bilateral acoustic neuromas

B. Brain hamartomas and ash-leaf skin patches

C. Capillary angiomas of the face and choroid

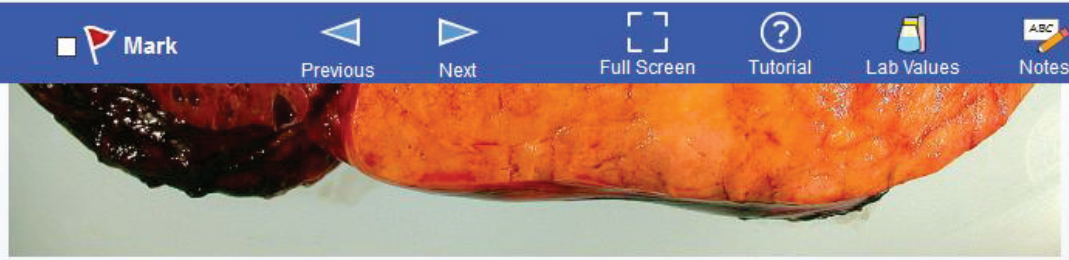
D. Cerebellar hemangioblastomas and liver cysts

E. Multiple peripheral neurofibromas and café-au-lait skin spots

F. Multiple telangiectasias of the skin and mucosa

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16



Histopathologic evaluation shows that the mass is composed of fat, smooth muscle, and blood vessels.
This patient is most likely to have which of the following additional findings?

A. ~~Bilateral acoustic neuromas~~ (4%)
B. Brain hamartomas and ash-leaf skin patches (45%)
C. ~~Capillary angiomas of the face and choroid~~ (5%)
D. ~~Cerebellar hemangioblastomas and liver cysts~~ (30%)
E. ~~Multiple peripheral neurofibromas and café-au-lait skin spots~~ (9%)
F. Multiple telangiectasias of the skin and mucosa (5%)

Incorrect
Correct answer

45%
02 mins, 34 secs
01/30/2021

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Renal angiomyolipoma is a benign tumor composed of blood vessels (angio), smooth muscle (myo), and fat (lipoma). These tumors can be diagnosed with an abdominal CT scan as the radiodensity of fat is less than that of water.

Angiomyolipomas are associated with **tuberous sclerosis**. In patients with bilateral renal angiomyolipomas, the incidence of tuberous sclerosis is 80%-90%. Tuberous sclerosis is an **autosomal dominant** condition characterized by cortical tubers and subependymal **hamartomas** in the brain, with consequent seizures and cognitive disability. Cardiac rhabdomyomas, facial angiofibromas, and leaf-shaped patches of skin lacking pigment (ash-leaf patches) can also occur.

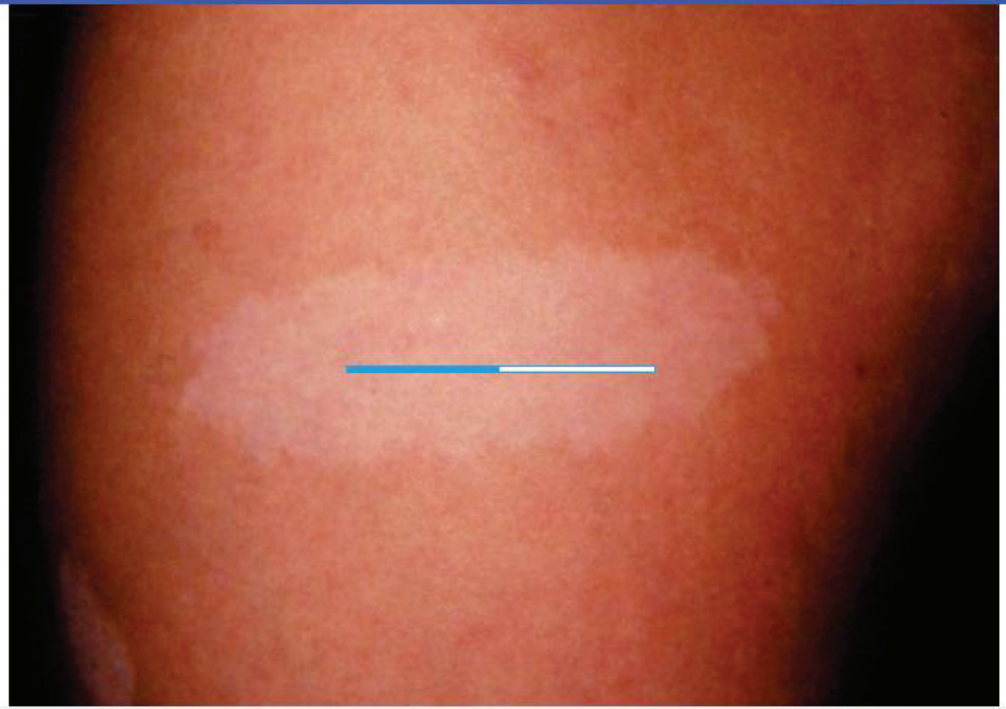
(Choice A) Neurofibromatosis type 2 is an autosomal dominant disorder marked by bilateral acoustic neuromas. These patients may also develop multiple meningiomas, gliomas, and ependymomas of the spinal cord.

(Choice C) Sturge-Weber syndrome is a rare congenital vascular disorder characterized by a facial port-wine stain and leptomeningeal capillary-venous malformation.

(Choice D) Cerebellar hemangioblastomas, retinal hemangiomas, and liver cysts are seen in von Hippel-Lindau disease, an autosomal dominant condition. These patients are at high risk for bilateral renal cell carcinomas.

1
2
3
4
5
6
7
• 8
• 9
• 10
• 11
• 12
• 13
• 14
• 15
• 16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

carcinomas

(Choice D) Cerebellar hemangioblastomas, retinal hemangiomas, and liver cysts are seen in von Hippel-Lindau disease, an autosomal dominant condition. These patients are at high risk for bilateral renal cell carcinomas.

(Choice E) Neurofibromatosis type 1 is an autosomal dominant disorder characterized by neurofibromas (plexiform and solitary), optic gliomas, pigmented nodules of the iris (Lisch nodules), and cutaneous hyperpigmented macules (café-au-lait spots).

(Choice F) Patients with hereditary hemorrhagic telangiectasia (also called Osler-Weber-Rendu syndrome) develop multiple telangiectasias of the skin and mucosa. The typical presentation is recurrent epistaxis or gastrointestinal bleeding (melena).

Educational objective:

Renal angiomyolipoma is a benign tumor composed of blood vessels, smooth muscle, and fat. Bilateral renal angiomyolipomas are associated with tuberous sclerosis, an autosomal dominant condition.

References

- Tuberous sclerosis complex and renal angiomyolipoma: case report and review of the literature.
- Pictorial review of tuberous sclerosis in various organs.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 10-year-old girl is brought to clinic for laboratory follow-up. Her mother was recently diagnosed with von Hippel-Lindau (VHL) disease, and the patient received genetic testing. Examination is unremarkable. Laboratory evaluation reveals a missense mutation in the *VHL* gene. Periodic surveillance with which of the following is most likely to be of benefit in this patient?

A. Bone marrow evaluation
B. Chest radiography
C. Colonoscopy
D. Echocardiography
E. Plasma metanephrines

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 10-year-old girl is brought to clinic for laboratory follow-up. Her mother was recently diagnosed with von Hippel-Lindau (VHL) disease, and the patient received genetic testing. Examination is unremarkable. Laboratory evaluation reveals a missense mutation in the *VHL* gene. Periodic surveillance with which of the following is most likely to be of benefit in this patient?

A. Bone marrow evaluation (6%)
B. Chest radiography (4%)
C. Colonoscopy (10%)
D. Echocardiography (4%)
✓ E. Plasma metanephrines (74%)

Correct
74% Answered correctly
51 secs Time Spent
11/09/2020 Last Updated

Explanation

Von Hippel-Lindau disease	
Etiology	• Mutation in the *VHL* tumor suppressor gene on chromosome 3 • Autosomal dominant inheritance
Manifestations	• Cerebellar & retinal hemangioblastomas • Pheochromocytoma • Renal cell carcinoma (clear cell subtype)
Management	• Surveillance for associated malignancies ◦ Eye/retinal examination ◦ Plasma or urine metanephrines ◦ MRI of the brain & spine ◦ MRI of the abdomen • Tumor resection

Von Hippel-Lindau (VHL) disease is an **autosomal dominant** condition caused by a loss-of-function mutation in the *VHL* gene on chromosome 3. The *VHL* gene product is a tumor suppressor protein that promotes degradation of damaged proteins and aids in cell cycle regulation. Similar to other disorders

Von Hippel-Lindau (VHL) disease is an **autosomal dominant** condition caused by a loss-of-function mutation in the *VHL* gene on chromosome 3. The *VHL* gene product is a tumor suppressor protein that promotes degradation of damaged proteins and aids in cell cycle regulation. Similar to other disorders affecting tumor suppressor genes (eg, familial retinoblastoma), a second, somatic mutation in this gene leads to the development of various **benign and malignant tumors** (eg, cerebellar and retinal hemangioblastomas, pheochromocytomas, renal cell carcinomas) with potentially serious complications.

Pheochromocytoma is a rare neoplasm arising from the adrenal medulla that can produce catecholamines (eg, epinephrine, norepinephrine). Patients may have hypertension, tachycardia, and sweating due to sympathetic overactivity; however, many are asymptomatic. As such, annual screening for increased urinary or **plasma metanephrines** (catecholamine breakdown products) is recommended. Likewise, screening for hemangioblastomas and renal cell carcinoma can be achieved with regular MRI and retinal examinations.

(Choice A) The results of bone marrow evaluation would be abnormal in patients with leukemia, which is not associated with VHL disease.

(Choice B) Chest radiography can identify lung metastases in a patient with a known malignancy. This patient requires evaluation for primary associated neoplasms before screening for metastases.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

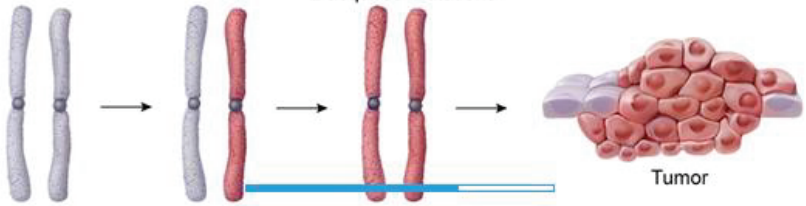
Von Hippel-Lindau (VHL) disease is an **autosomal dominant** condition caused by a loss-of-function

Exhibit Display

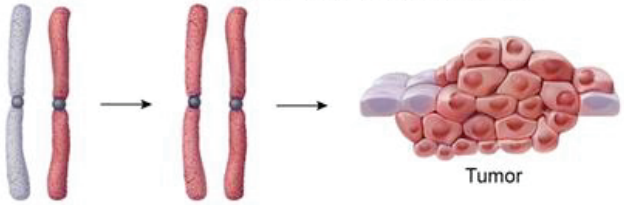
Knudson's 2-hit hypothesis

Both copies of the gene must be knocked out to promote malignancy.

Sporadic cancer:
2 acquired mutations



Hereditary cancer:
1 inherited and 1 acuired mutation



©UWorld

Zoom In | Zoom Out | Reset | New | Existing | My Notebook

(Choice C) Colonoscopy is performed in patients with an inherited predisposition to colorectal cancer, such as those with hereditary nonpolyposis colorectal cancer (ie, Lynch syndrome) and familial adenomatous polyposis. VHL disease is not associated with an increased risk of colorectal cancer in younger patients.

(Choice D) Screening echocardiography is performed in patients with tuberous sclerosis complex to identify an associated cardiac rhabdomyoma. Cardiac tumors are not a significant feature of VHL disease.

Educational objective:

Von Hippel-Lindau (VHL) disease is an autosomal dominant condition caused by a mutation in a tumor suppressor gene, which is associated with the development of pheochromocytomas, retinal and cerebellar hemangioblastomas, and renal cell carcinomas. Because of the potential for serious complications from these tumors, patients with VHL should receive annual surveillance, including plasma metanephrines, abdominal imaging, ophthalmologic examination, and MRI of the brain and spine.

References

- Pheochromocytoma screening initiation and frequency in von Hippel-Lindau syndrome.
- Von Hippel-Lindau disease.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 54-year-old man is admitted to the hospital following a high-speed motor vehicle accident. He is found to have right leg long bone fractures requiring open reduction/internal fixation. After the patient is stabilized, he is transferred to a skilled nursing facility for an extended rehabilitation period. During his stay at the facility, his right leg is immobilized for several weeks. The patient's management is complicated by decreased nutritional intake due to side effects from opioid pain medications. Measurement of his thigh following removal of casting materials finds a 2-centimeter decrease in diameter during the time of immobilization. This change in body measurement is due to a pathologic process similar to that seen in which of the following?

A. Adrenal glands during prolonged glucocorticoid therapy
B. Endometrial tissue during estrogen replacement therapy
C. Esophageal mucosa upon repeated acid exposure
D. Heart muscle during long-standing hypertension
E. Lung tissue after prolonged tobacco smoke exposure

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

have right leg long bone fractures requiring open reduction/internal fixation. After the patient is stabilized, he is transferred to a skilled nursing facility for an extended rehabilitation period. During his stay at the facility, his right leg is immobilized for several weeks. The patient's management is complicated by decreased nutritional intake due to side effects from opioid pain medications. Measurement of his thigh following removal of casting materials finds a 2-centimeter decrease in diameter during the time of immobilization. This change in body measurement is due to a pathologic process similar to that seen in which of the following?

A. Adrenal glands during prolonged glucocorticoid therapy (92%)
B. ~~Endometrial tissue during estrogen replacement therapy~~ (2%)
C. ~~Esophageal mucosa upon repeated acid exposure~~ (0%)
D. ~~Heart muscle during long-standing hypertension~~ (2%)
E. ~~Lung tissue after prolonged tobacco smoke exposure~~ (1%)

Correct

92%
02 mins, 10 secs
01/16/2021

This patient experienced decreased physical workload when his leg was immobilized. As a result, the skeletal muscle fibers in his leg decreased in size, leading to **disuse atrophy**. Atrophy is tissue loss due to **cellular death** or **reduced cell size**. It may be physiologic (eg, atrophy of Wolffian ducts in the female fetus, atrophy of maternal uterus following childbirth) or pathologic. Pathologic atrophy can be due to lack of use, loss of hormonal or neurologic stimulation (denervation atrophy), impaired circulation, mechanical compression, aging, or nutritional insufficiency. Pathologic atrophy may be local or generalized. On a cellular level, atrophy is seen as a reduction in mitochondria and rough endoplasmic reticulum. Muscular atrophy is characterized by decreased protein synthesis and loss of myofibrils. In prolonged atrophic states, **apoptosis** can lead to reduced cellular numbers.

Pathologic atrophy is also seen in the adrenal cortex during prolonged glucocorticoid use due to suppression of ACTH release. This can lead to acute adrenal insufficiency if the exogenous glucocorticoid therapy is abruptly discontinued.

(Choice B) After menopause, falling estrogen levels can lead to atrophy of the breasts, endometrium, and vaginal mucosa. Conversely, estrogen replacement in these patients can cause endometrial hyperplasia unless combined with progesterone therapy.

(Choice C) In chronic gastroesophageal reflux, esophageal mucosa subjected to repeated acid exposure

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

vaginal mucosa. Conversely, estrogen replacement in these patients can cause endometrial hyperplasia unless combined with progesterone therapy.

(Choice C) In chronic gastroesophageal reflux, esophageal mucosa subjected to repeated acid exposure may undergo metaplasia. Squamous epithelium is replaced by columnar epithelium in a condition known as Barrett esophagus.

(Choice D) Heart muscle subjected to long-standing hypertension is prone to developing hypertrophy, not atrophy.

(Choice E) Prolonged exposure to tobacco smoke can induce metaplasia in the epithelium of the lung. Columnar epithelium may be replaced by squamous epithelium (squamous metaplasia) with an associated risk of squamous cell carcinoma.

Educational objective:
Pathologic atrophy can be caused by decreased physical workload, loss of innervation, decreased blood supply, inadequate nutrition, absent endocrine stimulation, aging, or mechanical pressure.

References

- Disuse-induced muscle wasting.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 21-year-old man comes to the emergency department after suffering an injury during a football game. He was falling to the ground when he was struck forcefully from behind by the helmet of an opposing player. The patient was able to ambulate after the injury but has since had severe pain worsened by deep breaths. His blood pressure is 110/65 mm Hg, pulse is 110/min, and respirations are 16/min. On examination, there is bruising and tenderness over the left posterior chest wall. There is normal spinal range of motion and no midline tenderness. Gait and lower extremity neurologic examination are normal. Imaging studies reveal a fracture of the left 12th rib. Which of the following structures is most likely to be lacerated by the fractured bone?

A. Left hepatic lobe
B. Left kidney
C. Pancreas
D. Spleen
E. Visceral pleura

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

was falling to the ground when he was struck forcefully from behind by the helmet of an opposing player. The patient was able to ambulate after the injury but has since had severe pain worsened by deep breaths. His blood pressure is 110/65 mm Hg, pulse is 110/min, and respirations are 16/min. On examination, there is bruising and tenderness over the left posterior chest wall. There is normal spinal range of motion and no midline tenderness. Gait and lower extremity neurologic examination are normal. Imaging studies reveal a fracture of the left 12th rib. Which of the following structures is most likely to be lacerated by the fractured bone?

A. Left hepatic lobe (1%)
B. Left kidney (55%)
C. ~~Pancreas~~ (0%)
D. Spleen (33%)
E. ~~Visceral pleura~~ (8%)

Correct

55%

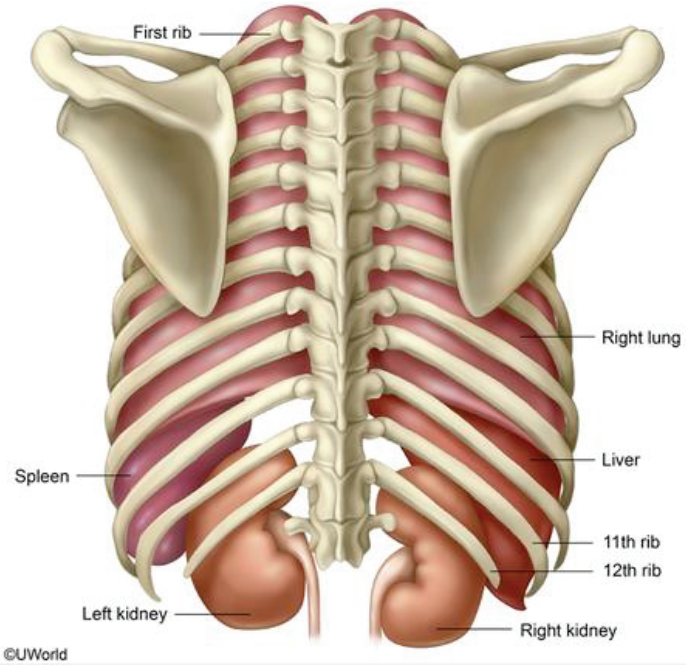
01 min, 16 secs

01/15/2021

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Posterior view of ribs & underlying organs



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

The first 7 rib pairs are considered "true" ribs because their costal cartilage attaches directly to the sternum; the cartilage of the lower 5 pairs does not, and they are considered "false" ribs. Of these, the cartilage of ribs 8-10 attaches to the costal cartilage of the upper ribs. The 11th and 12th ribs are "floating" ribs, meaning that they are not bound to the anterior rib cage by cartilage.

The **left 12th rib** overlies the parietal pleura medially and the **kidney** laterally. For this reason, the distal tip of the left 12th rib can be displaced into the retroperitoneum when fractured, lacerating the left kidney.

(Choice A) The liver occupies much of the right upper quadrant of the abdominal cavity, where the 8th-11th ribs overlie the liver's posterior surface. The left lobe crosses the midline antero-inferior to the diaphragm, where it is not vulnerable to a displaced fragment from the 12th rib.

(Choice C) The pancreas is a partially retroperitoneal organ that overlies the body of the second lumbar vertebra. Crushing abdominal trauma is the injury most likely to cause pancreatic damage.

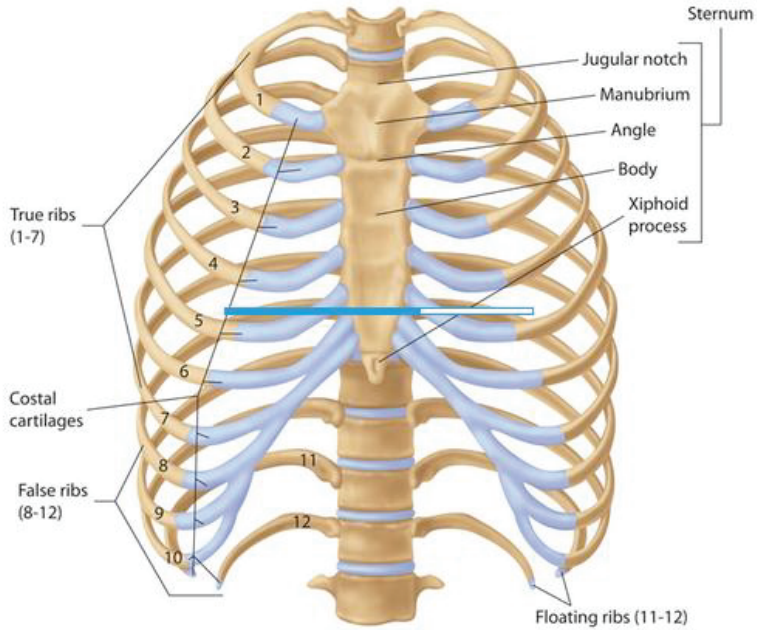
(Choice D) The spleen lies in the posterior superior portion of the left abdominal cavity. The left 9th, 10th, and 11th ribs overlie the spleen.

(Choice E) The visceral pleura envelop the lungs. At rest, the inferior margin of the left lung lies at the level of the 10th rib in the mid-scapular line. During maximal inhalation, the lung may descend to the level of the most medial portion of the 12th rib, but fractures of ribs 1-6 have the greatest chance of damaging

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Rib cage, anterior view



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

of the most medial portion of the 12th rib, but fractures of ribs 1-6 have the greatest chance of damaging

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

diaphragm, where it is not vulnerable to a displaced fragment from the 12th rib.

(Choice C) The pancreas is a partially retroperitoneal organ that overlies the body of the second lumbar vertebra. Crushing abdominal trauma is the injury most likely to cause pancreatic damage.

(Choice D) The spleen lies in the posterior superior portion of the left abdominal cavity. The left 9th, 10th, and 11th ribs overlie the spleen.

(Choice E) The visceral pleura envelop the lungs. At rest, the inferior margin of the left lung lies at the level of the 10th rib in the mid-scapular line. During maximal inhalation, the lung may descend to the level of the most medial portion of the 12th rib, but fractures of ribs 1-6 have the greatest chance of damaging the visceral pleura.

Educational objective:
The left kidney lies immediately deep to the tip of the 12th rib.

Anatomy	Miscellaneous (Multisystem)	Rib fracture
Subject	System	Topic

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

In an animal experiment the levels of various endogenous compounds are measured in the spinal fluid after application of noxious stimuli. One of the compounds that increase as a result of the experiment is a pentapeptide with a strong affinity to delta- and mu-receptors. Which of the following substances is most likely to have a common molecular origin with the pentapeptide described above?

A. Prolactin
B. TSH
C. ACTH
D. Growth hormone
E. Vasopressin
F. Somatomedin C

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

In an animal experiment the levels of various endogenous compounds are measured in the spinal fluid after application of noxious stimuli. One of the compounds that increase as a result of the experiment is a pentapeptide with a strong affinity to delta- and mu-receptors. Which of the following substances is most likely to have a common molecular origin with the pentapeptide described above?

A. Prolactin (5%)
B. TSH (5%)
C. ACTH (29%)
D. Growth hormone (9%)
E. Vasopressin (13%)
F. Somatomedin C (36%)

Correct

29%
Answered correctly

27 secs
Time Spent

01/30/2021
Last Updated

Enkephalins, endorphins, and dynorphins are endogenous opioid peptides that are part of the body's naturally occurring opioid system. These endogenous peptides are released in response to noxious stimuli and bind to different opioid receptors to allow physiologic modulation of pain. Several different types of opioid receptors have been identified and include mu, delta, kappa, and N/OFQ receptors. Available narcotics like morphine and hydromorphone produce therapeutic analgesic effects by binding to mu receptors and modulating pain perception. Endogenous opioid peptides also play a significant role in gastrointestinal, endocrine, autonomic, and emotional function. Beta-endorphin is one endogenous opioid peptide that is derived from proopiomelanocortin (POMC). POMC is a polypeptide precursor that goes through enzymatic cleavage and modification to produce not only beta-endorphins, but also ACTH and MSH. The fact that beta-endorphin and ACTH are derived from the same precursor suggests that there may be a close physiological relationship between the stress axis and the opioid system.

(Choice A) Prolactin is a somatotropic hormone synthesized in the anterior pituitary and is responsible for breast development and milk production. It is structurally similar to growth hormone.

(Choice B) TSH is a glycoprotein hormone synthesized in the anterior pituitary and is responsible for stimulating the secretion of thyroid hormone. It is also responsible for growth of the thyroid gland.

(Choice D) Growth hormone belongs to the family of somatotropic hormones. It is synthesized in the

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

stimulating the secretion of thyroid hormone. It is also responsible for growth of the thyroid gland.

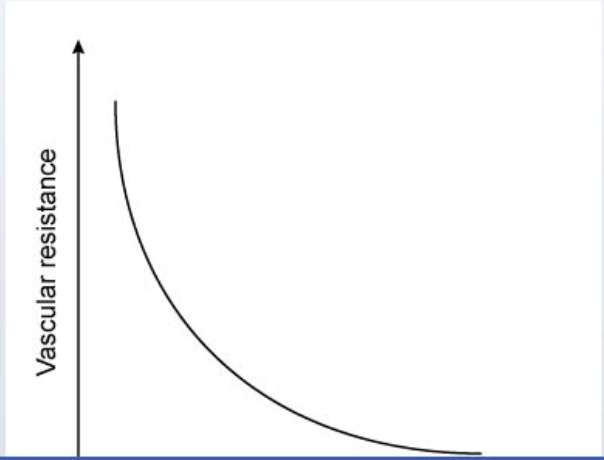
(Choice D) Growth hormone belongs to the family of somatotropic hormones. It is synthesized in the anterior pituitary and is responsible for overall body growth.

(Choice E) Vasopressin, also known as antidiuretic hormone (ADH), is a hormone synthesized in the hypothalamus and released from the posterior pituitary. It primarily functions to regulate fluid retention in the kidneys, but also causes arteriolar contraction of smooth muscle resulting in a pressor effect.

(Choice F) Somatomedin C is a peptide that is structurally similar to insulin. Also referred to as insulin like growth factor, somatomedin C is released in response to growth hormone and stimulates growth in target cells.

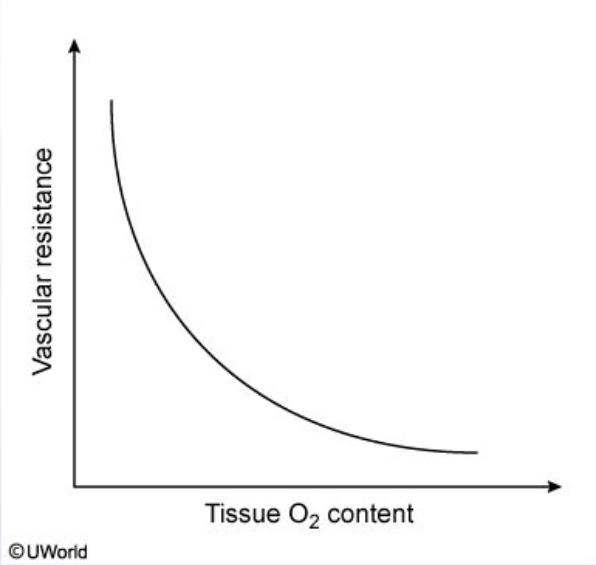
Educational Objective:
Beta-endorphin is one endogenous opioid peptide that is derived from proopiomelanocortin (POMC). POMC is a polypeptide precursor that goes through enzymatic cleavage and modification to produce not only beta-endorphins, but also ACTH and MSH. The fact that beta-endorphin and ACTH are derived from the same precursor suggests that there may be a close physiological relationship between the stress axis and the opioid system.

A researcher is conducting an experiment to determine factors affecting vascular resistance. Experiment animals are anesthetized, intubated, and attached to a controlled ventilation system. A catheter is placed into a small artery in various organs in each animal. The catheter is connected to a manometer for recording pressure and to an oximeter for continuous recording of oxygen saturation. The fraction of inspired oxygen is gradually changed, and arteriolar resistance is calculated from the manometer readings at regular intervals. The results shown below were most likely obtained from which of the following organs?



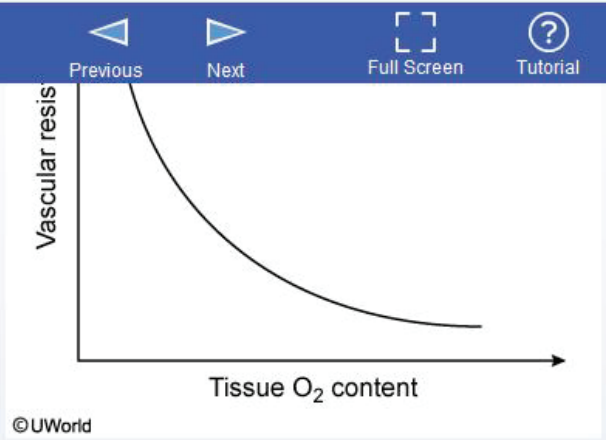
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

at regular intervals. The results shown below were most likely obtained from which of the following organs?



A. Brain
B. Heart
C. Kidneys

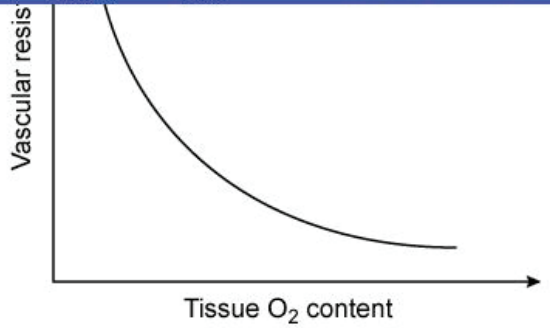
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16



A. Brain
B. Heart
C. Kidneys
D. Lungs
E. Small intestine

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16



A. Brain (10%)
B. Heart (5%)
C. Kidneys (4%)
D. Lungs (77%)
E. Small intestine (2%)

Correct

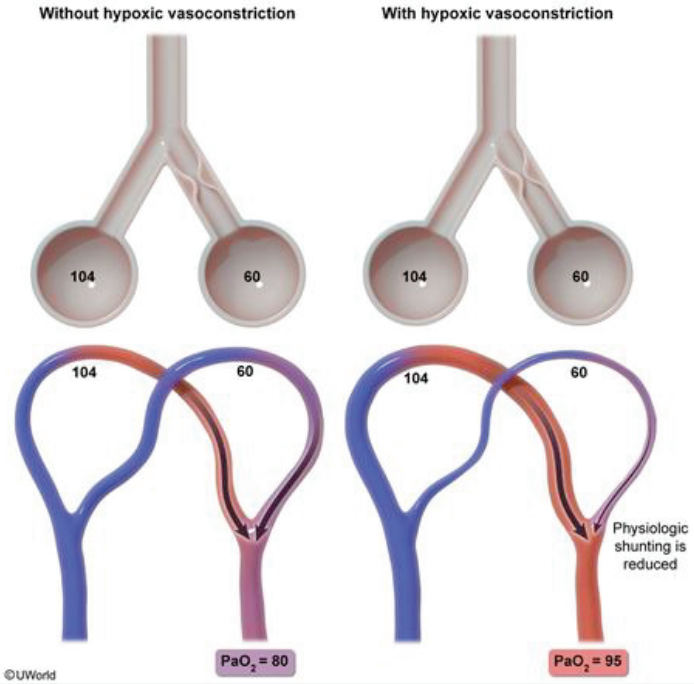
77%

19 secs

10/02/2020

1
2
3
4
5
6
7
8
9
10
11
12
• 13
• 14
• 15
• 16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

This graph depicts a vascular bed in which arterial/arteriolar resistance increases as the tissue O_2 content decreases. This response is unique to the **pulmonary vasculature**, in which **hypoxic vasoconstriction** occurs to divert blood flow away from underventilated lung regions and toward well-ventilated lung areas. This phenomenon **improves ventilation-perfusion mismatch** by decreasing physiologic shunting in poorly ventilated alveoli, leading to overall more **efficient gas exchange**. The relationship between hypoxia and vascular resistance is reversed throughout the rest of the body, ensuring that hypoxic organs and tissues receive increased blood flow.

(Choice A) Although the cerebral circulation is more sensitive to blood CO_2 levels (small degrees of hypercapnia lead to vasodilation), hypoxia causes significant arteriolar dilation when the partial pressure of oxygen (PO_2) falls below 50 mm Hg.

(Choice B) In the coronary vasculature, subendocardial blood flow is mediated by the local tissue PO_2, adenosine, prostacyclin, and nitric oxide. Decreased tissue PO_2 promotes vasodilation of arterioles in the myocardium.

(Choice C) A large increase in sympathetic tone may cause vasoconstriction of the renal vasculature, but hypoxia does not have this effect.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

(Choice B) In the coronary vasculature, subendocardial blood flow is mediated by the local tissue PO_2, adenosine, prostacyclin, and nitric oxide. Decreased tissue PO_2 promotes vasodilation of arterioles in the myocardium.

(Choice C) A large increase in sympathetic tone may cause vasoconstriction of the renal vasculature, but hypoxia does not have this effect.

(Choice E) Parasympathetic-induced intestinal vasodilation occurs in response to digestive chyme passing over intestinal mucosa. Sympathetic tone (not hypoxia) plays a large role in the splanchnic vasoconstriction that occurs with exercise or significant hypovolemia.

Educational objective:

The pulmonary vascular bed is unique in that tissue hypoxia results in a vasoconstrictive response. Such hypoxic vasoconstriction occurs in the small muscular pulmonary arteries to divert blood flow away from underventilated lung regions and toward well-ventilated lung areas to minimize ventilation-perfusion mismatch, leading to more efficient overall gas exchange.

References

- Hypoxic pulmonary vasoconstriction in humans.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 33-year old primigravida comes to the office to discuss results of prenatal testing. The patient is at 12 weeks gestation based on her last menstrual period. She has been taking prenatal vitamins inconsistently due to pregnancy-related nausea. Maternal alpha-fetoprotein level is reduced, and an ultrasound reveals increased nuchal translucency. Chorionic villous sampling shows a fetal karyotype of 47, XX, +21. The fetus is at greatest risk of developing which of the following conditions?

- A. Duodenal atresia
- B. Holoprosencephaly
- C. Myelomeningocele
- D. Nephroblastoma
- E. Omphalocele
- F. Pyloric stenosis

Submit

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 33-year old primigravida comes to the office to discuss results of prenatal testing. The patient is at 12 weeks gestation based on her last menstrual period. She has been taking prenatal vitamins inconsistently due to pregnancy-related nausea. Maternal alpha-fetoprotein level is reduced, and an ultrasound reveals increased nuchal translucency. Chorionic villous sampling shows a fetal karyotype of 47, XX, +21. The fetus is at greatest risk of developing which of the following conditions?

- A. Duodenal atresia (83%)
- B. ~~Holoprosencephaly~~ (2%)
- C. Myelomeningocele (4%)
- D. ~~Nephroblastoma~~ (1%)
- E. ~~Omphalocele~~ (3%)
- F. ~~Pyloric stenosis~~ (4%)

Correct

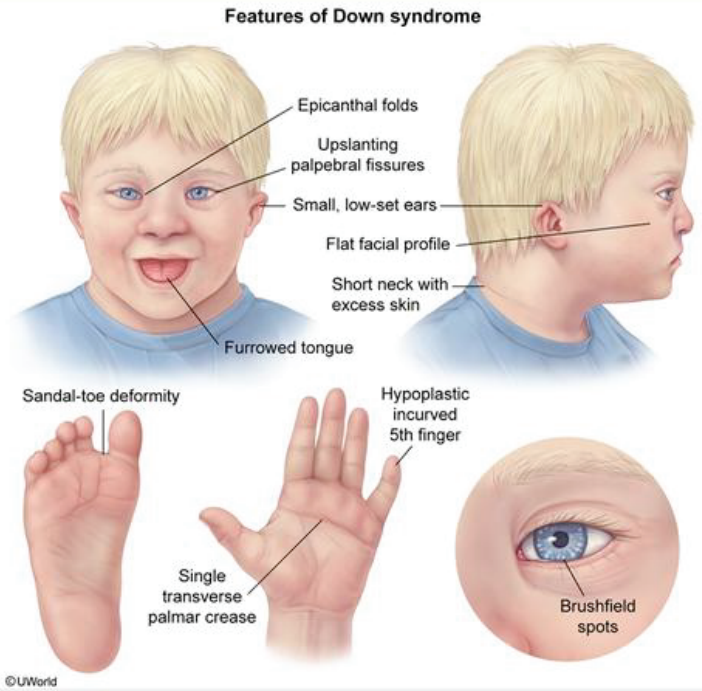
83% Answered correctly

50 secs Time Spent

02/20/2021 Last Updated

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Down syndrome (trisomy 21) is the most common trisomy in liveborn infants. The diagnosis is often suspected by prenatal screening (eg, **decreased maternal serum alpha-fetoprotein** [AFP]) and/or ultrasonography (eg, **increased nuchal translucency**) and confirmed by chorionic villous sampling or amniocentesis. Most cases are caused by meiotic nondisjunction due to maternal age ≥35, which result in 3 complete copies of chromosome 21.

Duodenal atresia, the failure of recanalization of the duodenum in early gestation, is the most common gastrointestinal abnormality associated with Down syndrome. Infants present during the first few days of life with bilious emesis and the classic "double-bubble" sign, which represents the dilated stomach and proximal duodenum. Patients with Down syndrome are also at risk for imperforate anus, Hirschsprung disease, tracheoesophageal fistula, and celiac disease.

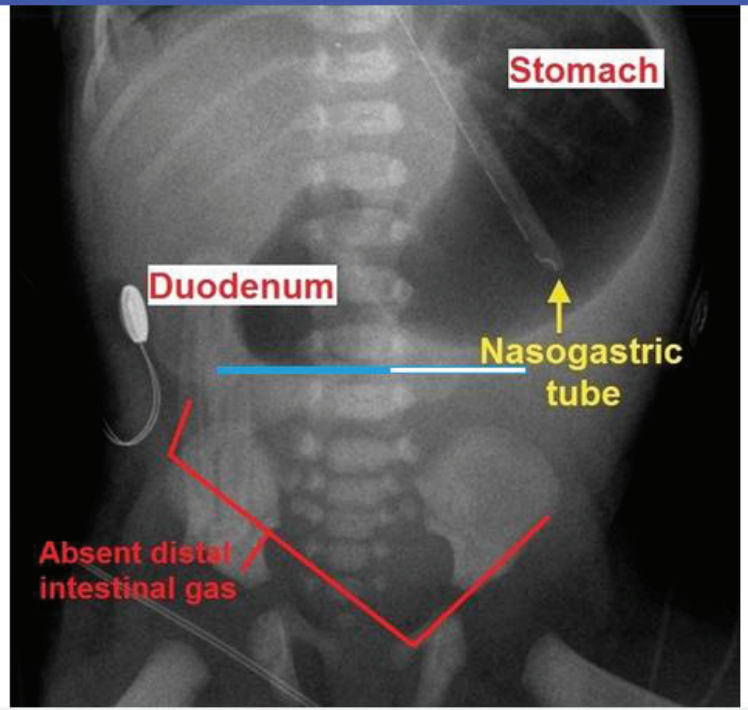
(Choice B) Holoprosencephaly, a severe developmental defect of the forebrain (prosencephalon), is associated with trisomy 13 (Patau syndrome). Additional features include microcephaly, microphthalmia, cleft lip/palate, and intellectual disability.

(Choices C and E) Markedly elevated AFP levels are associated with open neural tube and ventral wall defects (omphalocele, gastroschisis). Myelomeningocele is associated with trisomy 18, and omphalocele is associated with trisomies 13 and 18.

1
2
3
4
5
6
7
8
9
10
11
12
13
• 14
• 15
• 16

Down syndrome (trisomy 21) is the most common trisomy in liveborn infants. The diagnosis is often

Exhibit Display



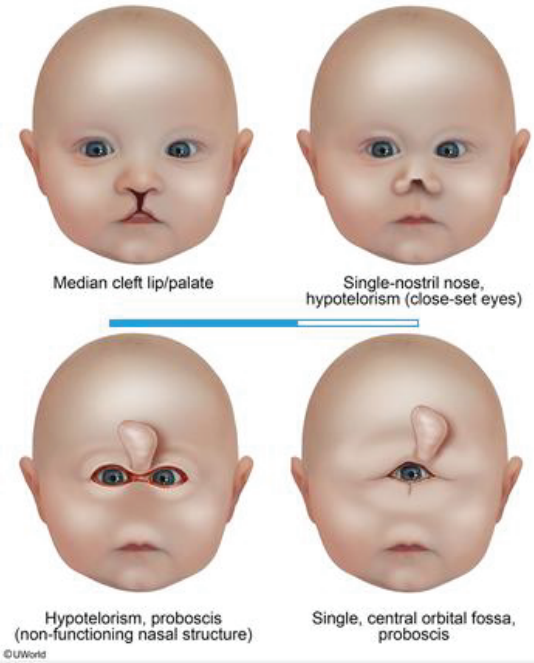
Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Down syndrome (trisomy 21) is the most common trisomy in liveborn infants. The diagnosis is often

Exhibit Display

Holoprosencephaly spectrum



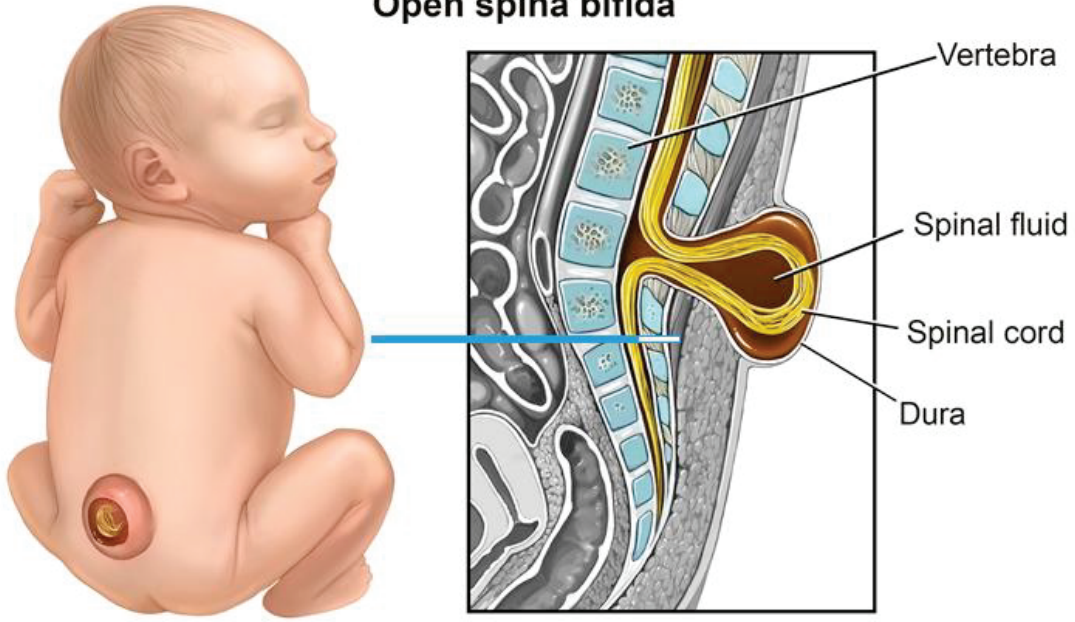
Zoom In
Zoom Out
Reset
New | Existing
My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
• 14
• 15
• 16

Down syndrome (trisomy 21) is the most common trisomy in liveborn infants. The diagnosis is often

Exhibit Display

Open spina bifida



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

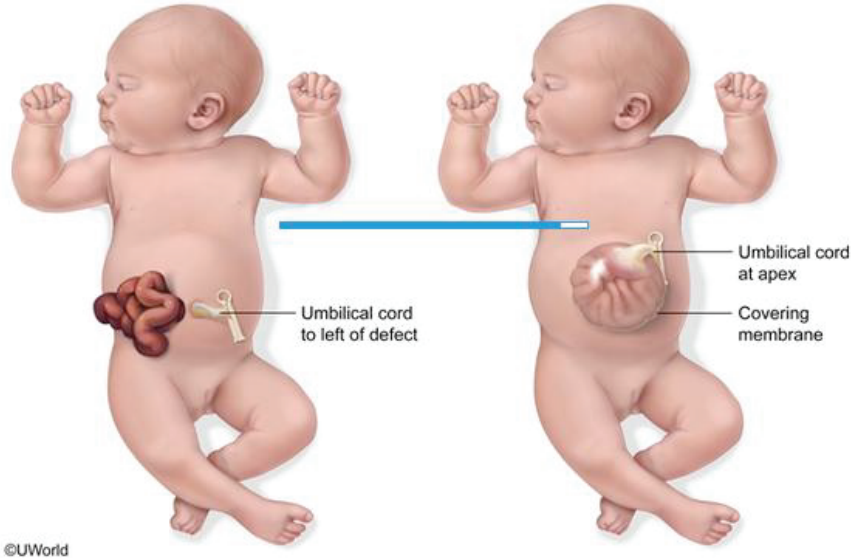
Down syndrome (trisomy 21) is the most common trisomy in liveborn infants. The diagnosis is often

Exhibit Display

Gastroschisis vs. omphalocele

Gastroschisis
Eviscerated bowel with no covering membrane

Omphalocele
Sac containing multiple organs



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

cleft lip/palate, and intellectual disability.

(Choices C and E) Markedly elevated AFP levels are associated with open neural tube and ventral wall defects (omphalocele, gastroschisis). Myelomeningocele is associated with trisomy 18, and omphalocele is associated with trisomies 13 and 18.

(Choice D) Nephroblastoma, or Wilms tumor, typically presents before age 5 with an abdominal mass. The majority of cases are sporadic, but a subset is associated with Beckwith-Wiedemann syndrome.

(Choice F) Pyloric stenosis is caused by hypertrophy of the pylorus and presents at age 3-6 weeks with forceful, nonbilious emesis. Pyloric stenosis is not associated with Down syndrome.

Educational objective:
Down syndrome (trisomy 21) is associated with decreased maternal serum alpha-fetoprotein and increased nuchal translucency. Duodenal atresia is the most common gastrointestinal complication in these patients.

References

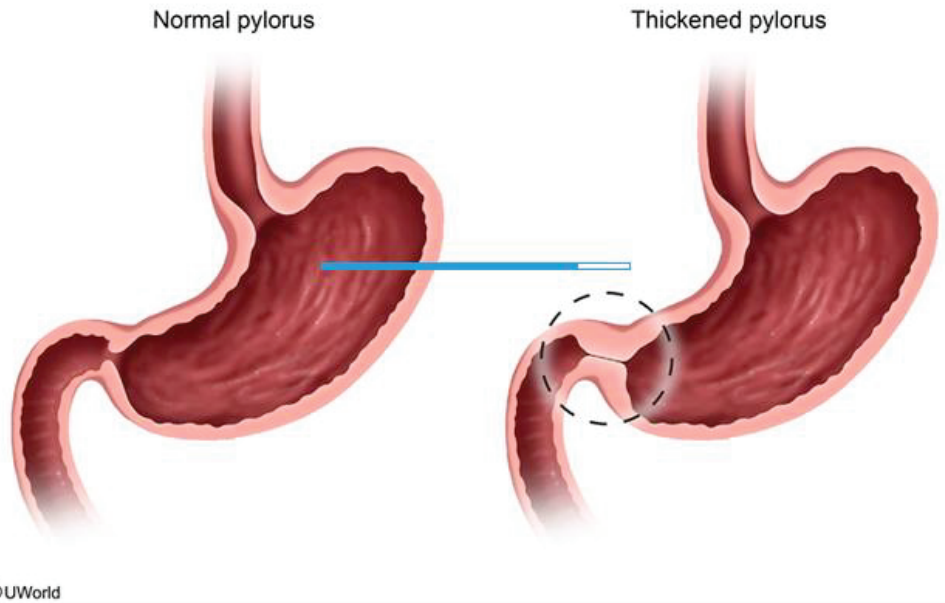
- Associated congenital anomalies among cases with Down syndrome.

Genetics	Miscellaneous (Multisystem)	Down syndrome
Subject	System	Topic

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Hypertrophic pyloric stenosis



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

Subject System Topic

1
2
3
4
5
6
7
8
9
10
11
12
13
• 14
• 15
• 16

A small-for-gestational-age infant is born prematurely to a 38-year-old woman who had inconsistent prenatal care. Physical examination shows a small head and eyes as well as a cleft lip and palate. There is a small, round punched-out lesion with an overlying thin membrane on the patient's scalp. A small, membranous sac with a loop of bowel protrudes from the patient's abdominal midline. The infant is transferred to the neonatal intensive care unit for further workup and management. Which of the following is most likely responsible for this patient's condition?

A. Down syndrome
B. Edwards syndrome
C. Maternal nicotine use
D. Maternal phenytoin ingestion
E. Maternal rubella infection
F. Patau syndrome
G. Williams syndrome

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

prenatal care. Physical examination shows a small head and eyes as well as a cleft lip and palate. There is a small, round punched-out lesion with an overlying thin membrane on the patient's scalp. A small, membranous sac with a loop of bowel protrudes from the patient's abdominal midline. The infant is transferred to the neonatal intensive care unit for further workup and management. Which of the following is most likely responsible for this patient's condition?

A. ~~Down syndrome~~ (5%)
B. ~~Edwards syndrome~~ (11%)
C. ~~Maternal nicotine use~~ (4%)
D. Maternal phenytoin ingestion (15%)
E. ~~Maternal rubella infection~~ (3%)
F. Patau syndrome (57%)
G. Williams syndrome (2%)

Correct

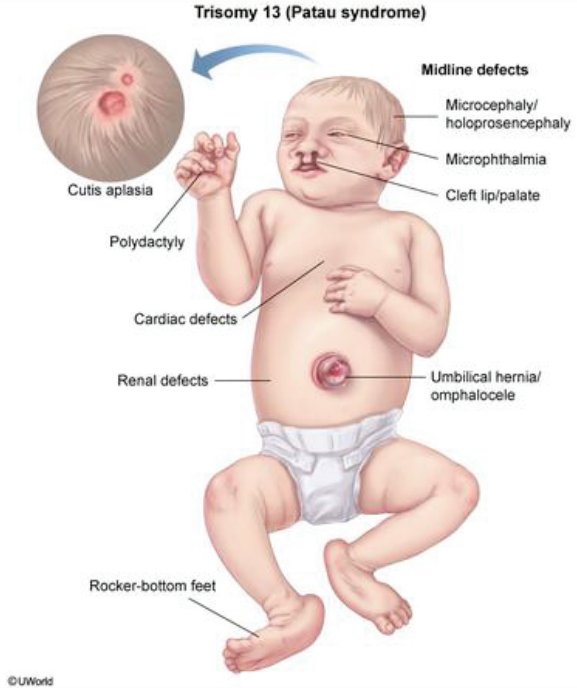
57%
Answered correctly

57 secs
Time Spent

10/12/2020
Last Updated

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

Patau syndrome, or **trisomy 13**, is a severe genetic disorder with phenotypic features reflecting a defect in the fusion of the **prechordal mesoderm**, an integral embryological structure affecting growth of the midface, eyes, and forebrain. This results in catastrophic midline defects, including holoprosencephaly, microcephaly, **microphthalmia**, **cleft lip/palate**, and omphalocele. Abnormal brain development results in intellectual disability and seizures. Additional abnormalities include **polydactyly** and **cutis aplasia** (focal skin defect of the scalp). The majority of patients with Patau syndrome die in utero; only 5% survive beyond 6 months.

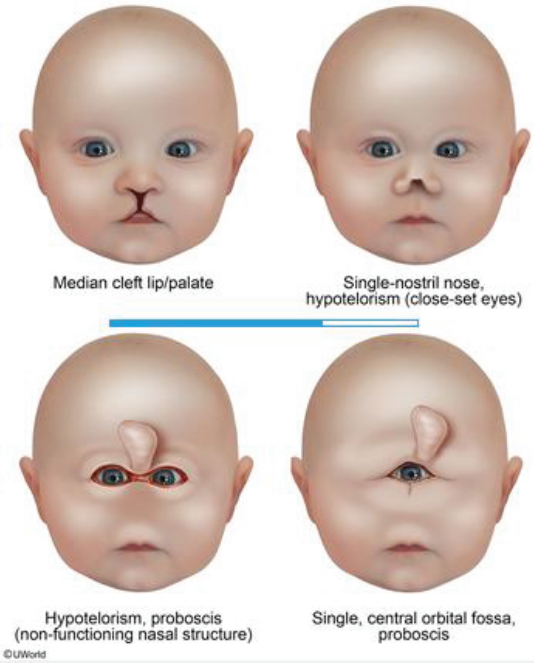
Cytogenetic studies usually demonstrate meiotic nondisjunction, which is the failure of chromosomal separation during meiosis, causing inheritance of a chromosome pair from 1 parent rather than a single chromatid. Maternal age ≥35 is an important risk factor for this abnormality of oocyte division. Nondisjunction results in a fetus with 3 complete copies of chromosome 13 (47, XX, +13).

(Choice A) Patients with Down syndrome (trisomy 21) typically have a flat facial profile, upslanting palpebral fissures, low-set small ears, redundant skin at the nape of the neck, single transverse palmar crease, and hypotonia. Increased rates of duodenal atresia and Hirschsprung disease are seen in these patients.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Holoprosencephaly spectrum

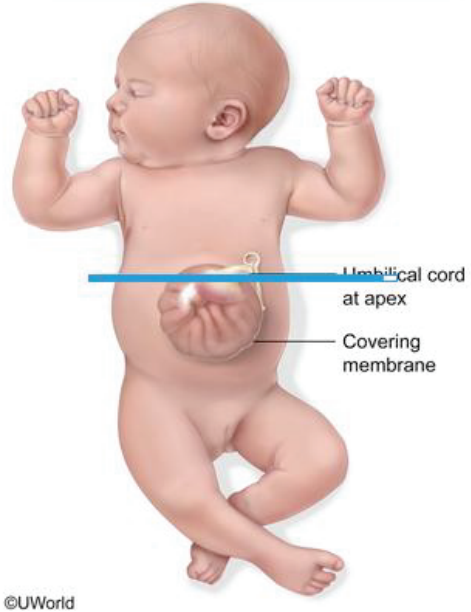


Zoom In
Zoom Out
Reset
New | Existing
My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
• 15
• 16

Exhibit Display

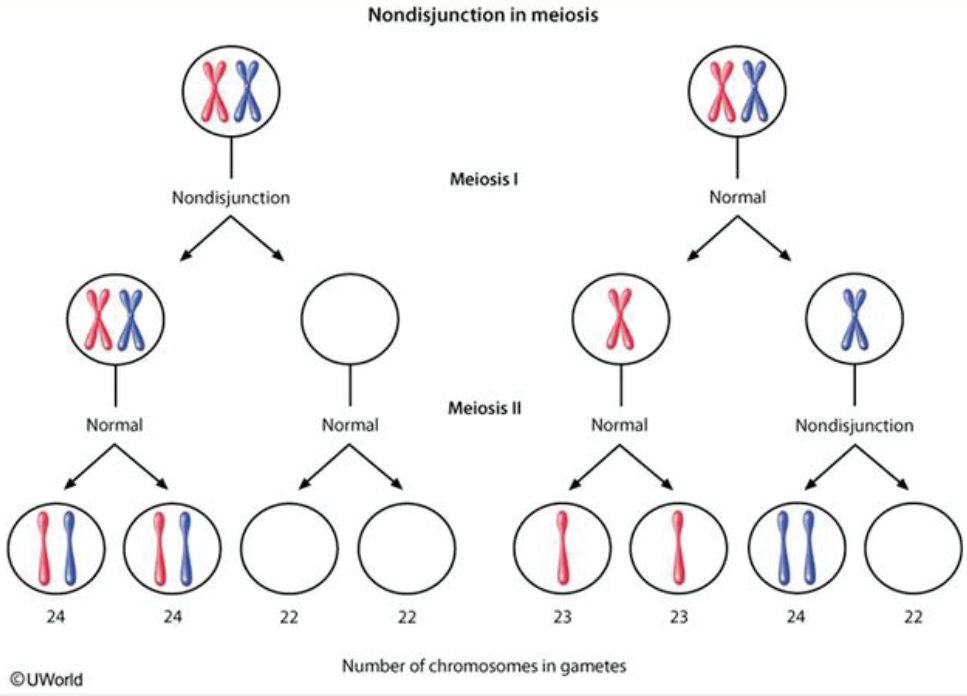
Omphalocele
Sac containing multiple organs



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

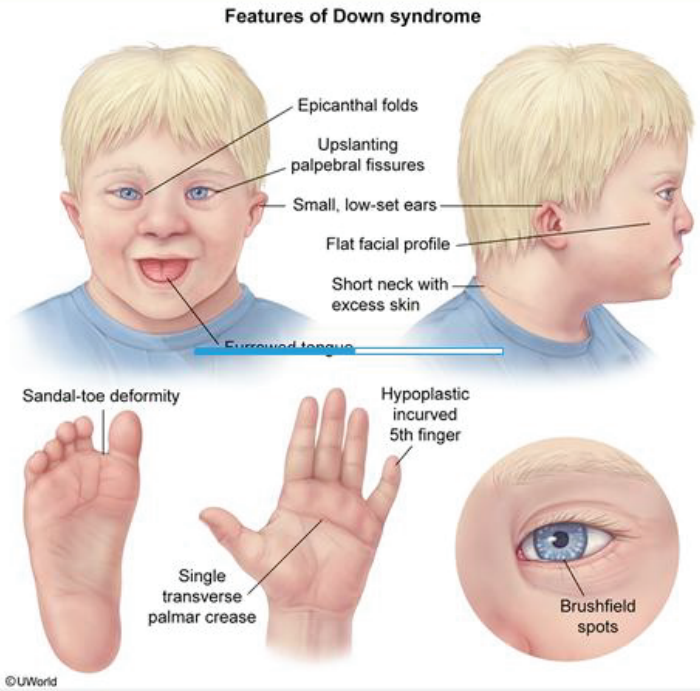
Exhibit Display



Zoom In
Zoom Out
Reset
New | Existing
My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

(Choice B) Clinical manifestations of Edwards syndrome (trisomy 18) include fetal growth retardation, hypertonia, micrognathia, and congenital heart defects. Additional features include clenched hands with overlapping fingers, Meckel's diverticulum, and malrotation.

(Choice C) Nicotine use during pregnancy increases the risk of prematurity and low birth weight. Related pregnancy complications include placenta previa and abruption.

(Choice D) Fetal exposure to maternal phenytoin has been associated with several congenital anomalies (eg, cardiac defects, cleft lip/palate, hypoplastic nails). It is not associated with cutis aplasia or omphalocele.

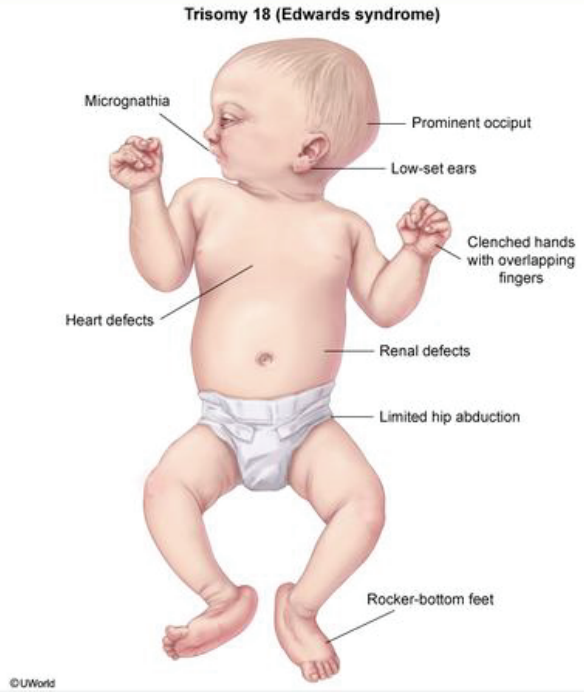
(Choice E) Congenital rubella syndrome typically occurs after a first trimester maternal rubella infection. Abnormalities classically include hearing loss, cataracts, and cardiac defects.

(Choice G) Williams syndrome is a genetic disorder classically associated with "elfin" facies, supravalvular aortic stenosis, and an extroverted personality.

Educational objective:
Patau syndrome (trisomy 13) usually occurs secondary to meiotic nondisjunction in mothers of advanced maternal age. Key physical findings reflect defective prechordal mesoderm fusion resulting in midline

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

(Choice C) Nicotine use during pregnancy increases the risk of prematurity and low birth weight. Related pregnancy complications include placenta previa and abruption.

(Choice D) Fetal exposure to maternal phenytoin has been associated with several congenital anomalies (eg, cardiac defects, cleft lip/palate, hypoplastic nails). It is not associated with cutis aplasia or omphalocele.

(Choice E) Congenital rubella syndrome typically occurs after a first trimester maternal rubella infection. Abnormalities classically include hearing loss, cataracts, and cardiac defects.

(Choice G) Williams syndrome is a genetic disorder classically associated with "elfin" facies, supravalvular aortic stenosis, and an extroverted personality.

Educational objective:
Patau syndrome (trisomy 13) usually occurs secondary to meiotic nondisjunction in mothers of advanced maternal age. Key physical findings reflect defective prechordal mesoderm fusion resulting in midline defects (eg, holoprosencephaly, microphthalmia, cleft lip/palate, omphalocele) as well as polydactyly and cutis aplasia.

References

- Clinical features and prognosis of a sample of patients with trisomy 13 (Patau syndrome) from Brazil.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A 48-year-old man comes to the office due to right inguinal discomfort. The patient first noticed "bumps" in his groin when he was dressing in the morning. He does not know how long they have been present but thinks they are relatively new. The patient was treated for gonorrhea several years ago but has no other medical problems. He drinks alcohol occasionally but does not use tobacco or illicit drugs. His mother died of metastatic melanoma. Cardiopulmonary examination is normal. The abdomen is soft and nontender. The right inguinal lymph nodes are enlarged and tender, as are several nodes in the right popliteal area. The distribution of lymphadenopathy in this patient would most likely be seen in which of the following conditions?

A. Asymmetric, hard prostate nodules
B. Firm, nontender right testicular mass
C. Large, irregular mole on the right great toe
D. Purulent laceration on the right lateral foot
E. Ulcerative lesion on the glans penis

his groin when he was dressing in the morning. He does not know how long they have been present but thinks they are relatively new. The patient was treated for gonorrhea several years ago but has no other medical problems. He drinks alcohol occasionally but does not use tobacco or illicit drugs. His mother died of metastatic melanoma. Cardiopulmonary examination is normal. The abdomen is soft and nontender. The right inguinal lymph nodes are enlarged and tender, as are several nodes in the right popliteal area. The distribution of lymphadenopathy in this patient would most likely be seen in which of the following conditions?

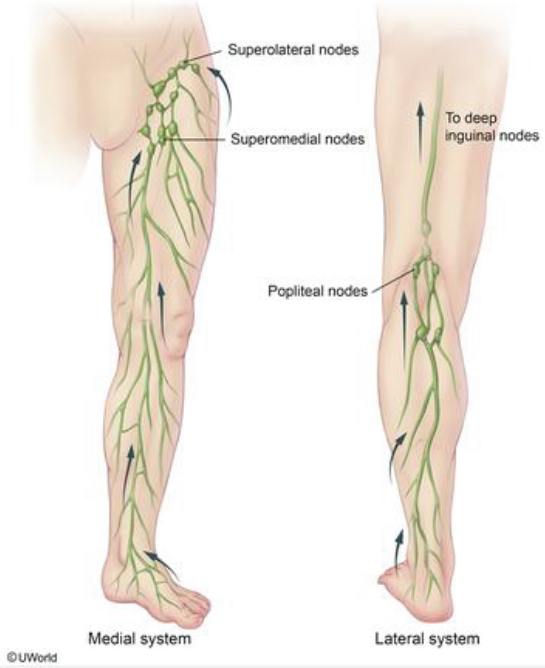
A. ~~Asymmetric, hard prostate nodules~~ (4%)
B. ~~Firm, nontender right testicular mass~~ (10%)
C. ~~Large, irregular mole on the right great toe~~ (20%)
D. Purulent laceration on the right lateral foot (43%)
E. Ulcerative lesion on the glans penis (20%)

Correct
43%
01 min, 32 secs
02/24/2021

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Exhibit Display

Lymphatic drainage of the lower extremity



Zoom In
Zoom Out
Reset
New | Existing
My Notebook

The **lymphatic system** of the extremities is divided into the superficial lymphatic vessels, which follow the venous system, and the deep lymphatic vessels, which follow the arterial system. The superficial vessels receive lymph from the skin and subcutaneous tissues, whereas the deep vessels drain both the deep muscles and the superficial vessels.

In the **lower extremities**, the superficial lymphatic system is divided into medial and **lateral tracks**. The medial track runs along the long saphenous vein up to the superficial inguinal lymph nodes, bypassing the popliteal nodes. Consequently, lesions on the medial foot cause inguinal lymphadenopathy **(Choice C)**. In contrast, lateral lesions, which drain via the lateral track and communicate with the popliteal and inguinal nodes, are more likely to cause lymphadenopathy in both the **popliteal and inguinal** areas.

(Choice A) Lymph from the prostate drains primarily into the internal iliac lymph nodes.

(Choice B) Lymph from the scrotum is drained into the superficial inguinal lymph nodes, and lymphatic vessels from the testes mirror the testicular arteries and drain into the para-aortic lymph nodes.

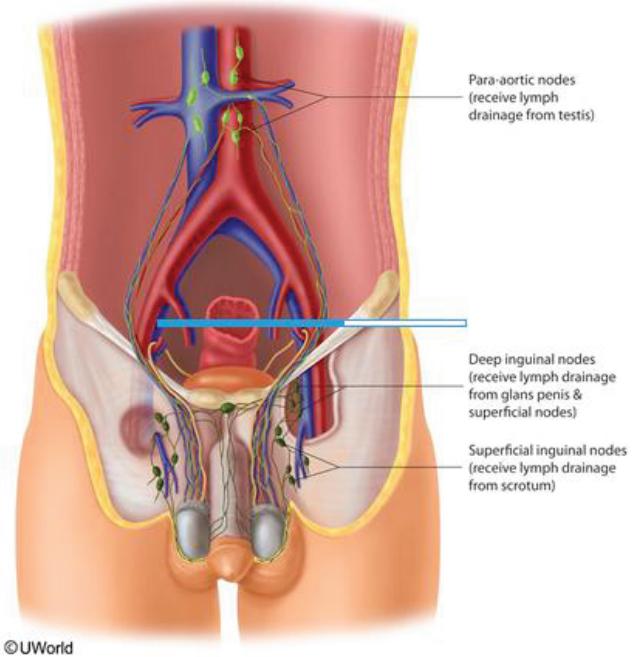
(Choice E) In addition to receiving drainage from the lower extremity, the superficial inguinal lymph nodes receive drainage from the scrotum (not testes), perineum, anterior abdominal wall (inferior to the umbilicus), buttocks, and skin of the penis. In contrast, the glans penis and penile urethra drain primarily via the deep lymphatic system into the deep inguinal nodes. The popliteal nodes would not be affected by

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

The lymphatic system of the extremities is divided into the superficial lymphatic vessels, which follow the

Exhibit Display

Lymph vessels & nodes of male genitalia



Zoom In | Zoom Out | Reset | New | Existing | My Notebook

(Choice B) Lymph from the scrotum is drained into the superficial inguinal lymph nodes, and lymphatic vessels from the testes mirror the testicular arteries and drain into the para-aortic lymph nodes.

(Choice E) In addition to receiving drainage from the lower extremity, the superficial inguinal lymph nodes receive drainage from the scrotum (not testes), perineum, anterior abdominal wall (inferior to the umbilicus), buttocks, and skin of the penis. In contrast, the glans penis and penile urethra drain primarily via the deep lymphatic system into the deep inguinal nodes. The popliteal nodes would not be affected by a lesion on the glans.

Educational objective:

In the lower extremities, the superficial lymphatic system is divided into medial and lateral tracks. The medial track runs up to the superficial inguinal lymph nodes, bypassing the popliteal nodes. Consequently, lesions on the medial foot cause inguinal lymphadenopathy, whereas lateral lesions are more likely to cause lymphadenopathy in both the popliteal and inguinal areas.

References

- Lymphoedema of the lower extremities—background, pathophysiology and diagnostic considerations.

Anatomy Miscellaneous (Multisystem) Lymphatic drainage

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

A boy is admitted to the neonatal intensive care unit shortly after being born to a 28-year-old woman who had poor prenatal care. His temperature is 37.2 C (99 F), blood pressure is 70/30 mm Hg, pulse is 128/min, and respirations are 40/min. Pulse oximetry shows 85% on room air. Physical examination is significant for orbital hypertelorism, a submucous cleft palate, and bifid uvula. An echocardiogram reveals right ventricular hypertrophy, pulmonary stenosis with ventricular septal defect, and overriding aorta. The patient's diagnosis is eventually confirmed by fluorescence in situ hybridization. These findings are most consistent with which of the following mechanisms?

A. Abnormal ciliary motility
B. Chromosome microdeletion
C. Defect in fibrillin synthesis
D. Genomic imprinting
E. Mutation of tumor suppressor gene
F. Nucleotide repeat expansion

had poor prenatal care. His temperature is 37.2 C (99 F), blood pressure is 70/30 mm Hg, pulse is 128/min, and respirations are 40/min. Pulse oximetry shows 85% on room air. Physical examination is significant for orbital hypertelorism, a submucous cleft palate, and bifid uvula. An echocardiogram reveals right ventricular hypertrophy, pulmonary stenosis with ventricular septal defect, and overriding aorta. The patient's diagnosis is eventually confirmed by fluorescence in situ hybridization. These findings are most consistent with which of the following mechanisms?

A. Abnormal ciliary motility (3%)
B. Chromosome microdeletion (78%)
C. Defect in fibrillin synthesis (4%)
D. Genomic imprinting (5%)
E. Mutation of tumor suppressor gene (1%)
F. Nucleotide repeat expansion (5%)

Correct
78%
02 mins, 07 secs
02/23/2021

DiGeorge syndrome/velocardiofacial syndrome	
Pathogenesis	• Chromosome 22q11.2 deletion • Defective development of pharyngeal pouches
Clinical features	• **C**onotruncal **c**ardiac defects (tetralogy of Fallot, truncus arteriosus, interrupted aortic arch) • **A**bnormal facies • **T**hymic hypoplasia/aplasia (**T**-cell deficiency) • **C**raniofacial deformities (**c**left palate) • **H**ypocalcemia/**H**ypoparathyroidism

Chromosome 22q11.2 **microdeletion** involves deletion of genes residing in adjacent loci. This results in variable phenotypes including **DiGeorge syndrome** (cardiac anomalies, hypoplastic/absent thymus, hypocalcemia) and **velocardiofacial syndrome** (cleft palate, cardiac anomalies, dysmorphic facies); the latter is exemplified in this patient.

Defective **neural crest migration** into derivatives of the **third** and **fourth** pharyngeal pouches results in maldevelopment of the thymus and parathyroid as well as subsequent T-cell deficiency and hypocalcemia.

latter is exemplified in this patient.

Defective **neural crest migration** into derivatives of the **third** and **fourth** pharyngeal pouches results in maldevelopment of the thymus and parathyroid as well as subsequent T-cell deficiency and hypocalcemia. Cardiac defects include interrupted aortic arch and tetralogy of Fallot (described in this patient). Dysmorphic facial features include orbital hypertelorism, short palpebral fissures and short philtrum, cleft palate, and bifid uvula. In **fluorescence in situ hybridization** (the gold standard test), genes of interest are hybridized with fluorescently labeled DNA probe. Lack of fluorescent signal is indicative of a microdeletion.

(Choice A) Kartagener syndrome results from immotile cilia due to an autosomal recessive microtubular defect in the dynein arm. It results in infertility, situs inversus, chronic sinusitis, and bronchiectasis.

(Choice C) Marfan syndrome, a fibrillin defect, causes cystic medial necrosis of the aorta and joint hyperextensibility. It is not associated with a cleft palate, but rather with a high-arched palate with crowded teeth and a narrow face.

(Choice D) Microdeletion syndrome due to genomic imprinting includes Prader-Willi syndrome (PWS) and Angelman syndrome (AS). In PWS, paternal genes are deleted (15q-) and maternal genes are silenced, resulting in short stature, obesity, hypotonia, and hypogonadism. In AS, maternal genes are deleted (15q-)

Angelman syndrome (AS). In PWS, paternal genes are deleted (15q-) and maternal genes are silenced, resulting in short stature, obesity, hypotonia, and hypogonadism. In AS, maternal genes are deleted (15q-) and paternal genes are silenced. Patients have microcephaly, ataxia, hand flapping movements, and frequent laughter ("happy puppet").

(Choice E) Tuberous sclerosis involves defective tumor suppressor gene-coded proteins hamartin (*TSC1*) and tuberin (*TSC2*), and is characterized by cutaneous angiofibromas, brain hamartomas, and cardiac rhabdomyomas.

(Choice F) Friedrich ataxia (GAA repeat) is characterized by spinocerebellar degeneration and spinal ataxia. It is not associated with facial or palatal malformations. Other examples of trinucleotide repeats include Fragile X (CGG) and myotonic dystrophy (CTG).

Educational objective:
Chromosome 22q11.2 microdeletion results in DiGeorge syndrome (cardiac anomalies, hypoplastic or absent thymus, and hypocalcemia) and velocardiofacial syndrome (cleft palate, cardiac anomalies, dysmorphic facies). Fluorescence in situ hybridization is the "gold standard" for detecting a microdeletion.

References